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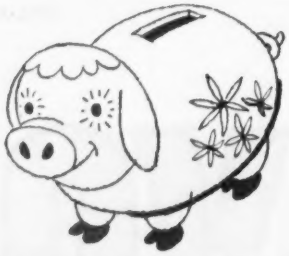

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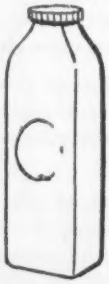

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1. Segal, M.S., et al.: Advances in the Physiology and Treatment of Bronchial Asthma, Quart. Rev. Allergy & Applied Immunology 6:399 (December) 1952.

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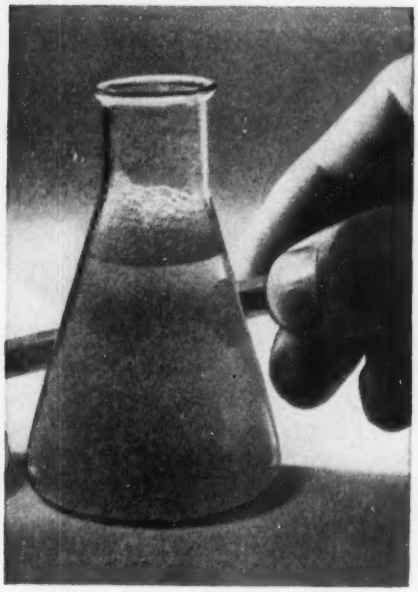

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1. *American Medical Association: New and Nonofficial Remedies, 1954. J. B. Lippincott Co., Philadelphia, p. 147*
2. *Scott, R. L., and others: Antibiot. & Chemo. 4:691 (June) 1954*

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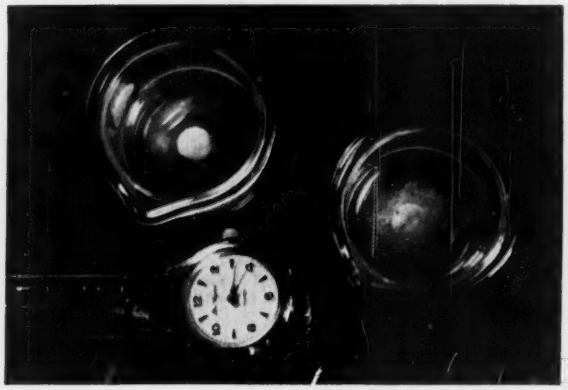
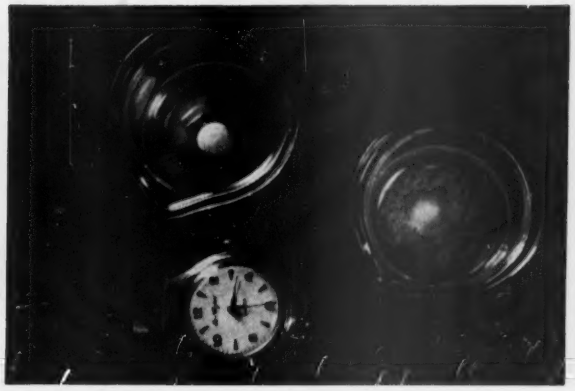
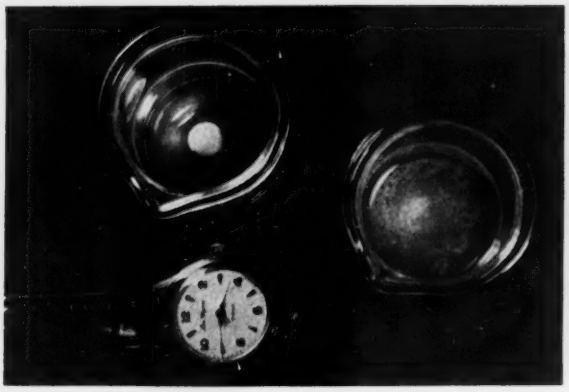


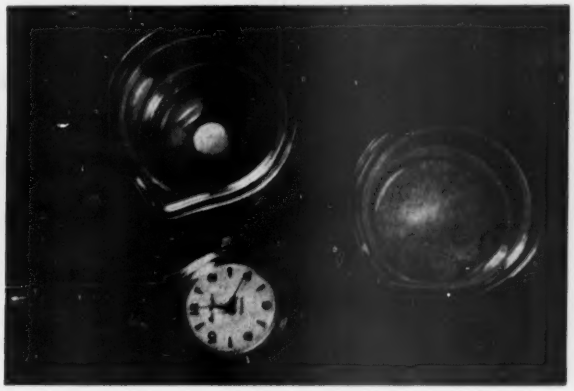
3:20—Five minutes later, *Filmtab** coating has already started to disintegrate. The tissue-thin film actually begins to dissolve within 30 seconds after patient swallows tablet.



3:30—*Filmtab** is now completely dissolved. At this stage, ERYTHROCIN is ready to be absorbed, and ready to destroy sensitive cocci—even those resistant to other antibiotics.



3:45—Now the *Filmtab** tablet mushrooms out with all of the drug available for absorption. Note that enteric-coated tablet is still intact. Tests show that the new Stearate form definitely protects ERYTHROCIN against gastric acids.



4:00—Because of *Filmtab** (marketed only by Abbott) the drug is released faster, absorbed sooner. In the body, effective ERYTHROCIN blood levels now appear *in less than 2 hours* (instead of 4-6 hours as before). Abbott

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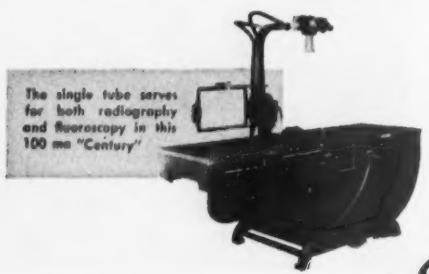

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Volume 251 OCTOBER 28, 1954 Number 18

ANGIOCARDIOGRAPHY*

A Guide to Mediastinal Exploration

STANLEY M. WYMAN, M.D.†

BOSTON

SURGICAL exploration of the mediastinum today can be accomplished with minimal risk, and yet a certain mortality and morbidity are inherent in the procedure. For this reason, the advantage of being able to determine without exploration the nature of a radiographic shadow in the mediastinum is apparent. If the shadow in question represents a vessel no corrective procedure may be needed, or surgery may be contraindicated because of the danger of injury to a vascular structure. Conversely, if a mediastinal mass is shown to be separate from the vascular system its nature can be identified only by histologic examination.

HISTORY

The earliest known investigations in opacifying the heart and great vessels in the thorax were undertaken by Forssmann in 1929,[1] when he introduced a ureteral catheter into the veins of his right arm and then into the superior vena cava and right atrium. He was unsuccessful in his attempt to visualize the right side of the heart by using sodium iodide solutions of 15 to 20 per cent.

The pulmonary vessels in a living human being were first outlined in 1931 by Moniz, de Carvalho and Lima.[1] They introduced 6 cc. of a 120 per cent sodium iodide solution by a catheter into the right atrium of the heart. Other investigators quickly adopted similar or more refined technics to improve on these early results. Among the earliest successful angiocardiograms made by injection of contrast material in the arm veins were those of Castellanos, Pereiras and Garcia, who, in 1926, presented the results of their work. They used "perabrodil" at first and later "uroselectan." Robb and Steinberg,[2] working with Soma Weiss during the years 1928 to 1933, became interested in various technics for accurately determining circulation time in patients with cardiac asthma. In 1935 and 1936, this work was amplified by animal studies at Bellevue Hospital. Subsequently, they discovered that they could visualize the pulmonary blood vessels in man utilizing commercially available 35 per cent Diodrast, concentrated by boiling to about 70 per cent. They introduced the technic of making serial radiographic exposures, and it is largely owing to their early work that angiocardiography as it is known today has been evolved.

METHOD

In this country the present commonly used method consists of an intravenous introduction of approximately 1 cc. of concentrated Urokon, Diodrast or Neoiopax per kilogram of body weight, the total quantity seldom exceeding 70 cc. This material is usually injected through a No. 12 Robb cannula, inserted by open dissection and tied into the basilic vein of the right arm. Before the contrast medium is injected, patency of the cannula and vein is maintained by intravenous infusion of saline solution. The contrast medium, often miscalled "dye," that has previously been warmed to body temperature is injected by a Robb syringe with a large, central-bore outlet, which is coupled to the cannula by a Luer–Lok adapter and flexible tubing. The injection is made as rapidly as possible, in most cases in less than two seconds. Serial films of the heart and central thorax are then made.

At the Massachusetts General Hospital a novel experimental device for obtaining serial films[3] has been in use for several years. It has proved to be of great value. In the near future, however, it will be replaced by a commercial apparatus that allows for many more exposures at rates up to 12 per second. Films can be made simultaneously in two planes at right angles to one another. Injections of contrast substance will be made by an automatic, gas-operated pressure apparatus attached to a catheter whose tip lies in the right ventricle or pulmonary artery.

ANGIOCARDIOGRAPHY AS A GUIDE IN MEDIASTINAL EXPLORATION

Early angiocardiographic investigations were di-

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rected principally toward the anatomy of the pulmonary arteries, but as the technic improved, attention was centered on the heart and the great systemic vessels. Much work has been done on congenital heart disease and anomalies of the great vessels, and this application of the method needs no further comment, its value being self-evident. More recently, interest has been aroused in the use of angiocardiography during the study of primary carcinoma of the lung. In some cases the method has proved of value in determining the possibility or impossibility of complete resection.[4]

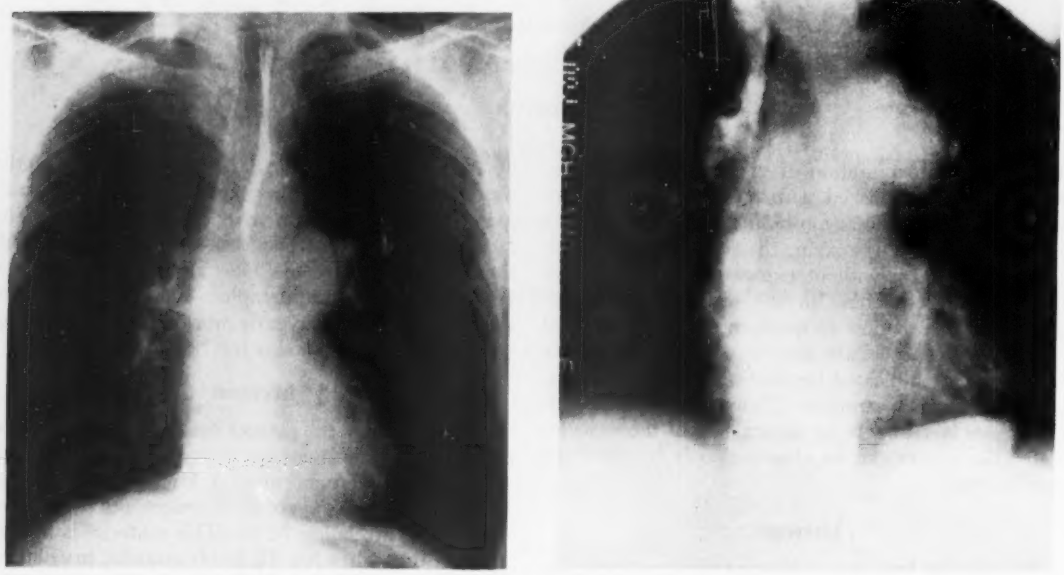

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FIGURE 1. *Roentgenographic Studies in Case 1.*
The conventional roentgenogram (A) *shows prominence of the left contour of the heart below the aortic arch. The angiocardiogram* (B) *reveals that this prominence represents dilatation of the pulmonary artery.*

The increasing use of x-ray examination of the chest, especially as a survey procedure, has uncovered many asymptomatic mediastinal and pulmonary lesions. Since the histologic nature of most peripheral lesions cannot be known without surgery, persons harboring such masses are usually — and justifiably — subjected to exploratory thoracotomy.[5]

The situation in centrally located mediastinal or juxtacardiac lesions is quite different. It is the intention of this report to emphasize the possibility, in many cases, of determining *without thoracotomy* whether such central shadows are a part of the cardiovascular system or are detached from the heart and great vessels.[6] From the patient's point of view this is tremendously important. If a questionable shadow becomes denser after injection of contrast material, its exact nature can be identified with a high degree of accuracy, and definitive surgery if indicated can be undertaken with assurance. On the other hand the anatomic situation demonstrated may require no correction and intervention may involve unwarranted hazard. This foreknowledge of what will be encountered can afford the surgeon an invaluable guide to any proposed exploration.

Conversely, if the shadow under consideration is proved to represent a mass separate from the cardiovascular system, some form of mediastinal lesion may be present, and histologic analysis is required for identification. In this instance, exact delineation of the adjacent vascular structures will be of great help in planning the surgical approach.

The cases reported below are presented to illustrate the value of angiocardiography as a guide in the problem of mediastinal exploration. It must be emphasized that much of the usefulness of angiocardiographic examination is derived from comparison of many films of the questionable area, each film showing progressive degrees of opacification of cardiovascular structures. Many changes are quite subtle and are recognized positively only by being seen a number of times in successive films. It is not possible to demonstrate in this publication the full extent of the data furnished by this method.

CASE REPORTS

CASE 1 (AJP U-780934). A 52-year-old man had always been in good health until 1 year before hospital entry, when, after the removal of his last 13 teeth, he began to lose weight and appetite. After consultation with his physician an x-ray examination of the chest was made. This disclosed an abnormality of the left contour of the heart in the region of the pulmonary artery (Fig. 1*A*), and fluoroscopic study suggested that expansile pulsation was present.

Bronchoscopic and physical examinations were negative.

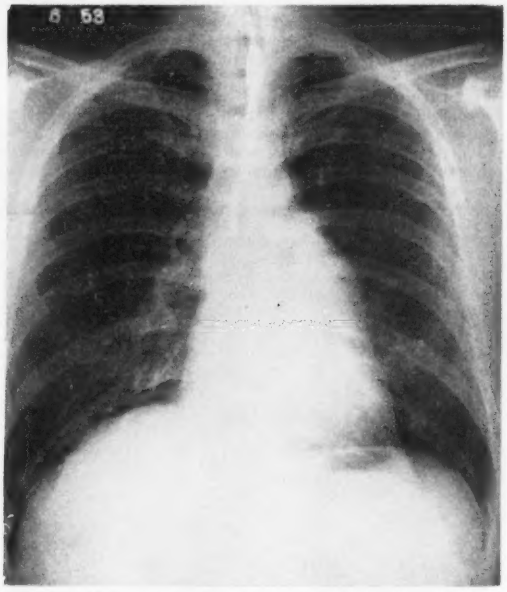

FIGURE 2. *Posteroanterior Roentgenogram in Case 2, Showing Prominence of the Left Border of the Heart, Slightly Lower in Location Than but Quite Similar to That in Figure 1.*

Since it could not be determined with certainty whether the unusual prominence of the heart shadow represented an enlarged main pulmonary artery or some form of mediastinal tumor, angiocardiography was done. This showed conclusively that the structure in question was an unusually large undivided pulmonary artery (Fig. 1*B*).

In view of the diagnosis, exploration, which might otherwise have been performed, was avoided. Exact identification of the juxtacardiac shadow revealed the technical impossibility of correcting the condition.

CASE 2 (AS P-233416).* A 42-year-old man was admitted to the hospital in January, 1953, for study of a chest abnormality detected in the previous November on a survey examination. There were no symptoms except for a nonproductive cough, which had been present for several years and was attributed to cigarette smoking.

Physical examination revealed no abnormalities.

Roentgenographic examination disclosed an unusually prominent left border of the heart close to the expected location of the main pulmonary artery and inseparable from it; there was doubt whether the pulsations noted were expansile or transmitted (Fig. 2).

Angiocardiography was performed to determine whether this shadow represented an enlarged pulmonary artery or a mass separate from the cardiovascular system. Films taken in the early phase of the examination (Fig. 3*A*) showed no increased opacification of the shadow, proving that the pulmonary artery and its major branches were uninvolved, and films taken with the left side of the heart and aorta opacified (Fig. 3*B*) demonstrated no connection between these structures and the mediastinal mass. It was evident that the shadow in question did not represent part of the cardiovascular system and was therefore some form of mediastinal abnormality.

Thoracotomy disclosed a mass of matted lymph nodes with 1 well circumscribed, 7-cm. node. The histologic diagnosis was hyperplasia and hypertrophy.

In contradistinction to Case 1 the indication for exploratory thoracotomy was strengthened by the demonstration that the area in question was not an in-

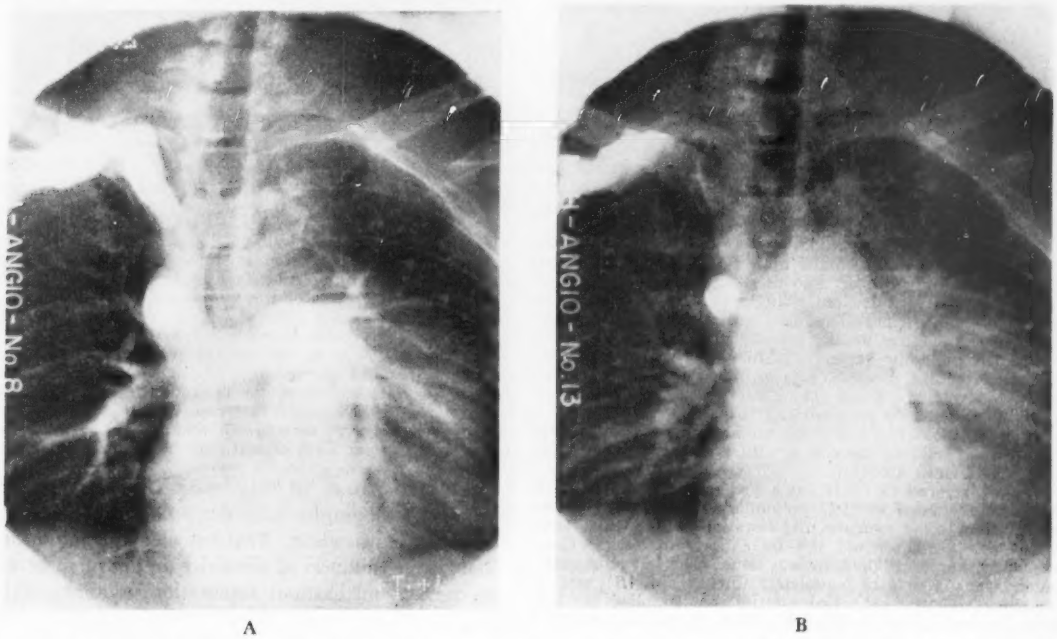

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FIGURE 3. *Angiocardiograms in the Phases of Pulmonary-Artery* (A) *and Aortic* (B) *Filling, Revealing No Density Change in the Area in Question.*
This proves that the lesion is not a part of the cardiovascular system.

*Previously reported.[7]

tegral part of the cardiovascular system. The possibility of pulmonary-artery aneurysm being thus eliminated, exploration to determine the nature of the mediastinal mass became virtually mandatory.

CASE 3 (AG U-799144). A 15-year-old boy was subjected to x-ray examination of the chest because of a vague chest discomfort, which was most pronounced when he lay down. The history otherwise was not remarkable, and general physical examination disclosed no abnormality.

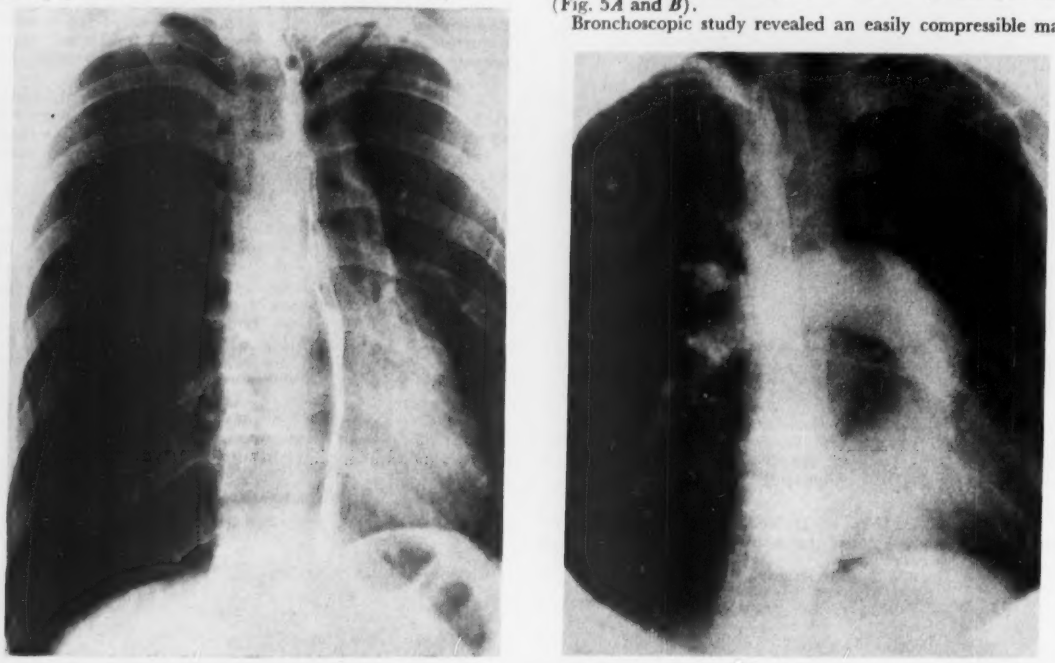

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FIGURE 4. *Films in Case 3 (Reproduced from Wyman[8] with the Permission of the Publishers).*
Conventional teleroentgenogram (A) *shows a small left hemithorax with elevation of the left leaf of the diaphragm and displacement of the heart to the left; the usual shadow produced by the large branching left pulmonary artery is absent. Angiocardiogram* (B) *discloses a large right pulmonary artery and absence of the left pulmonary-artery branch.*

Roentgenographic examination showed the left hemithorax to be somewhat smaller than the right; the heart and mediastinum were displaced to the left, and the left leaf of the diaphragm was elevated. The right lung revealed compensatory emphysema. The most striking feature was absence of the shadows usually produced by the large branches of the left pulmonary artery. In their place a fine network of lacy, vascular shadows, representing enlarged bronchial arteries, was seen. X-ray examination demonstrated no respiratory shift of the mediastinum (Fig. 4*A*).

Bronchoscopic study showed no abnormality except an unidentified weblike vascular structure in the distal portion of the left main bronchus.

It was believed that this was a case of congenital absence of the branches of the left pulmonary artery, but the possibility that some obscure manifestation of bronchial adenoma was present could not be entirely excluded. Consequently, angiocardiography was done. The left pulmonary artery was found to be completely absent (Fig. 4*B*), and in its place enlarged bronchial arteries that supplied the left lung were visualized in the late phases of the examination.[8]

The examination was of value in that it confirmed the diagnosis of an absent pulmonary artery and obviated the need of subjecting the patient to exploratory thoracotomy or further investigative procedures.

CASE 4 (RW U-815324). A 29-year-old Negress, referred from another hospital, complained of repeated episodes of shortness of breath on exertion and precordial pain of 4 years' duration. With these attacks, especially when she extended her head, she also experienced difficulty in swallowing.

Physical examination was within normal limits.

Roentgenographic examination disclosed a mass in the right upper part of the mediastinum just above the level of the aortic arch. This mass, which lay between the trachea and esophagus, was thought to show expansile pulsation (Fig. 5*A* and *B*).

Bronchoscopic study revealed an easily compressible mass indenting the posterior wall of the trachea; the overlying mucosa was normal. Esophagoscopic examination demonstrated a dark, compressible, pulsating mass indenting the anterior and left walls of the esophagus.

Although it seemed likely that this shadow represented some form of vascular anomaly arising from the aorta, it was considered wise to exclude the possibility of a tumor. Angiocardiography showed that the shadow became opacified in the late phases of the examination after the aorta had filled with the contrast material. A diagnosis of anomalous right subclavian artery with dilatation of its proximal portion, or of some form of aortic diverticulum was made.

The true nature of this lesion was demonstrated by angiocardiography, and the probable difficulty of correcting it was clear. This knowledge is important. Though the mildness of clinical symptoms had been a deterrent to mediastinal exploration, it might otherwise have come under consideration at a later date.

CASE 5 (CF U-834821). A 44-year-old woman, who was known to have had hypertension for 10 years, had had repeated epistaxes for the past 4 years. She had been a patient in a mental institution for some time, and was referred to this hospital because of an abnormality discovered in an x-ray examination of the chest.

Roentgenographic examination indicated a mass, measuring about 2 cm. in diameter and lying just above the arch of the aorta, from which it could be separated; it slightly displaced the esophagus anteriorly.

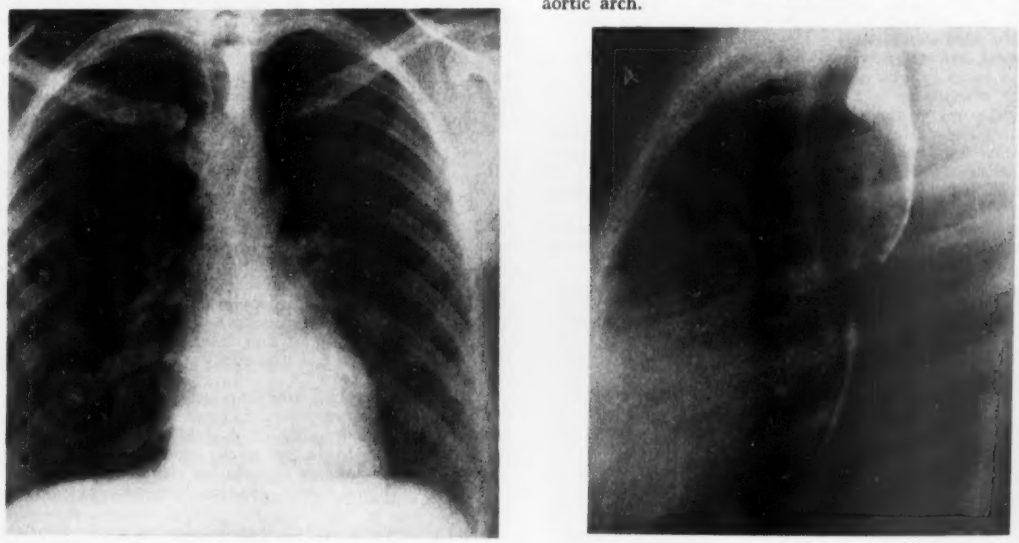

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FIGURE 5. *X-Ray Studies in Case 4.*

Conventional posteroanterior roentgenogram with barium in the esophagus (A) *reveals a rounded, dense shadow above and to the right of the aortic arch, causing moderate embarrassment of the esophagus. The lateral view* (B) *shows the mass to lie between the esophagus and the trachea and to indent both.*

Because of the impossibility of determining whether this shadow represented a vessel or some type of mediastinal tumor, angiocardiography was done. In contrast to Case 4 the lesion did not become denser, indicating that it was separate from the cardiovascular system and presumably represented some form of mediastinal mass that lay just behind the origin of the left subclavian artery and above the aortic arch.

If the patient had not been mentally disturbed, the angiocardiographic examination would have made her a candidate for exploratory surgery. At present no further action will be taken.

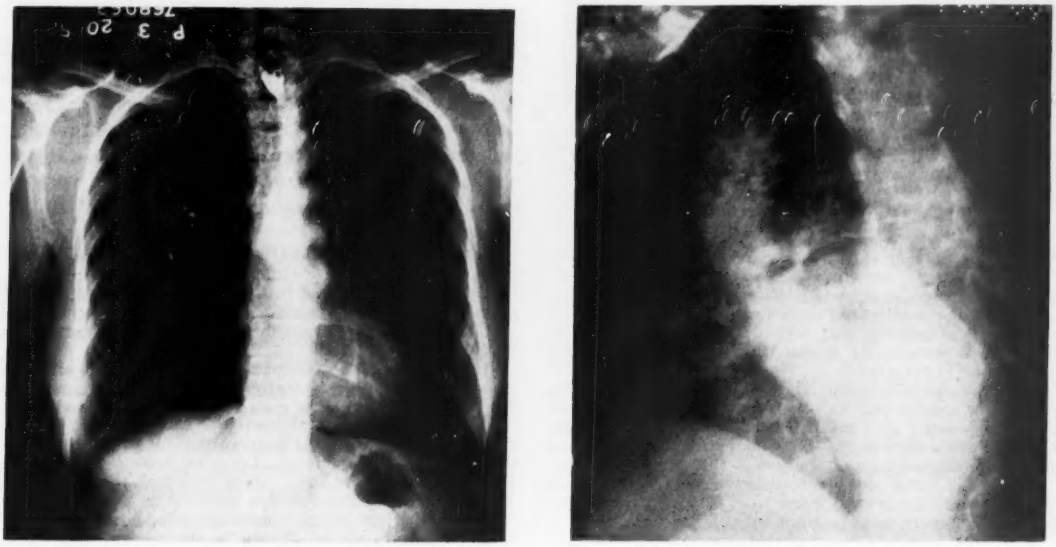

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FIGURE 6. *X-Ray Films in Case 6.*

An overpenetrated posteroanterior chest roentgenogram with barium in the esophagus (A) *shows a shadow in the mediastinum superimposed on the spine just below the aortic arch. An angiocardiogram in the right posterior oblique position* (B) *reveals contrast material in the aorta and coarctation, with aneurysmal dilatation of the aorta distal to the coarctation.*

CASE 6 (AH U-768063-B). A 37-year-old woman was admitted to the hospital for study of a mediastinal abnor-

mality that had been discovered on a survey roentgenographic examination. A diagnosis of intramural, extramucosal tumor of the esophagus had been made elsewhere, and she was referred to a thoracic surgeon at this hospital for study and treatment.

Physical examination was not remarkable except for a Grade 4 early systolic murmur, heard in the left 2d and 3d anterior interspaces and transmitted over the anterior and posterior parts of the chest. There was no diastolic component. (The patient was known to have had a heart murmur since the age of 10, but she had been active in sports and had developed normally.) Peripheral pulsations in the arms and legs were normal. Initial blood-pressure readings were 150/82 (right arm) and 170/100 (right leg).

Esophagoscopic study revealed no abnormality. Bronchoscopic inspection showed protrusion into the lumen of the

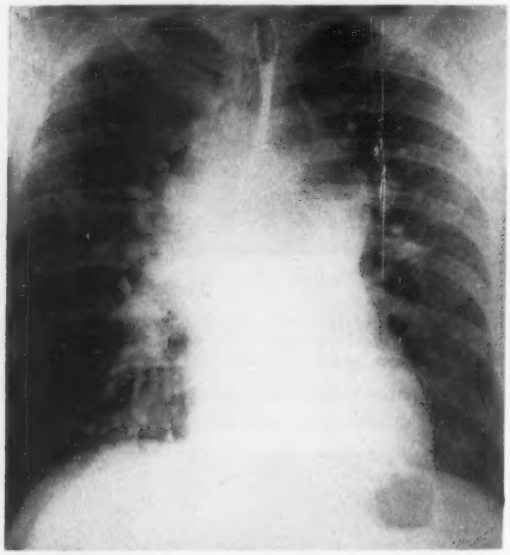

FIGURE 7. *Teleroentgenogram in Case 7, Demonstrating the Typical Figure-8 Silhouette Formed by the Enlarged Right Superior Vena Cava, Persistent Left Superior Vena Cava and the Heart Shadow.*

The pulmonary arteries are greatly engorged.

membranous portion of the trachea just above the coryna.

Roentgenoscopic and conventional roentgenographic examinations, including a barium study of the esophagus, suggested that the mediastinal mass represented the dilatation of the aorta commonly seen beyond a point of coarctation, and that its irregularity might be due to an aneurysmal component (Fig. 6*A*).

Angiocardiographic examination (Fig. 6*B*) established the presence of coarctation of the upper thoracic aorta just beyond the origin of the left subclavian artery. The poststenotic portion showed a distinct nodularity consistent with aneurysmal dilatation.[9]

Subsequent blood-pressure readings showed that pressure in the legs was consistently lower than that in the arms, and the original report was therefore believed to be in error.

Contrast studies established an exact diagnosis in this case. Because of the patient's age, the lack of serious symptoms and the probable existence of degenerative changes and aneurysmal dilatation of the distal aorta no attempt at surgical correction of the coarctation was undertaken.

CASE 7 (FRW U-794337-B). Congenital heart disease had been recognized at birth because of cyanosis in this 26-year-old man. This had caused but slight restriction of activity, and he had been able to participate in most sports except tennis and basketball.

Physical examination showed mild cyanosis and clubbing of the fingers and toes. The heart was considerably enlarged, with a Grade 1 systolic murmur at the apex and a Grade 2 systolic murmur over the pulmonic area. The pulmonic 2d sound was greater than the aortic. The blood pressure was 130/100; on 2 occasions the hemoglobin was 26 gm. per 100 cc.

Roentgenographic examination demonstrated great widening of the superior mediastinum, with convexity to each side. This, added to the shadow of the enlarged heart below, formed a figure-8 outline. Roentgenoscopic study showed wide pulsation of the right side of the mediastinum, and this was thought to be due to an enlarged, tortuous aorta. The pulmonary vessels, which were enlarged, disclosed increased amplitude of pulsation (Fig. 7).

A definite diagnosis could not be reached from conventional roentgenographic inspection alone, although the presence of congenital heart disease was evident. The figure-8 configuration of the heart and great vessels is quite typical of anomalous drainage of pulmonary veins into the persistent left superior vena cava.[10,11]

Electrocardiographic study revealed hypertrophy and strain of the right ventricle. It seemed unlikely that there could be any abnormality in the chest besides congenital heart disease, but to determine the type of cardiac anomaly and at the same time to exclude the remote possibility of a superior mediastinal tumor, angiocardiographic examination was done.

The examination showed that the shadow in the right side of the mediastinum, originally thought to be made by the aorta, was actually formed by a very large superior vena cava that was filled from a tremendously enlarged persistent left superior vena cava, which in turn received a great flow of blood from the upper portion of the left upper lobe. This observation was further confirmed by cardiac catheterization, which demonstrated an abnormally high amount of oxygen in the superior vena cava. On some films contrast substance appeared to enter the aorta before the left ventricle was opacified, possibly accounting for the clinical cyanosis.

In this case it was obvious that the congenital heart disease was predominantly one of abnormal return of blood from the lungs to the superior vena cava and that at the present time no corrective procedure could be performed. The angiocardiographic examination eliminated the possibility, however unlikely, of a coexisting mediastinal tumor.

CASE 8 (M McC U-817605). One month before hospital admission a 5-year-old girl, who had previously been asymptomatic, was found to have a very slight, high-pitched apical systolic heart murmur. After a negative electrocardiographic examination at another hospital she was referred to this hospital for study.

Roentgenographic examination, including roentgenoscopy, showed a shadow in the anterior superior mediastinum that might have represented a mass or a prominent vessel.

General physical examination was within normal limits.

The cardiac consultant believed that, other than the murmur, there was no evidence of organic heart disease; various observers were unable to agree whether the mediastinal shadow represented a vascular anomaly or a mass.

During the course of 7 months periodic x-ray examinations demonstrated no change in the shadow and careful roentgenoscopic inspection disclosed no change in its size on deep inspiration. Physical examinations remained as on admission.

Angiocardiographic study showed the superior vena cava to be displaced to the right, and the aorta slightly to the left, with a space between. Thus, a mass apart from the vascular system and separating the vena cava and aorta was postulated.

Angiocardiography strengthened the decision for mediastinal exploration by establishing a diagnosis of a

mediastinal mass. Thoracotomy disclosed an enlarged thymus.

CASE 9 (BMC U-815700). A 66-year-old man entered the hospital because of dysphagia of 2 months' duration accompanied by pain radiating to the right side of the neck and behind the right ear. Esophagoscopic inspection and biopsy done at another hospital had revealed the presence of a squamous-cell carcinoma of the esophagus.

Esophagoscopic and roentgenographic examinations at the Massachusetts General Hospital showed no abnormality except for a small primary carcinoma of the upper cervical esophagus. Below the tumor and just above the aortic arch, the left posterior aspect of the esophagus was indented by an extrinsic mass, but there was no evidence of mucosal involvement. A healed duodenal ulcer, which was apparently causing no difficulty, was also found. The aorta was moderately tortuous, suggesting atherosclerosis.

The diagnosis of primary carcinoma of the upper esophagus was clear, but there was some question concerning the nature of the mass lying above the aortic arch and indenting the posterior aspect of the esophagus. Although it was thought that this represented an aberrant right subclavian artery arising as the last branch from the aortic arch and crossing behind the esophagus, there was a possibility that it represented an enlarged lymph node secondary to the primary tumor, or some other form of mediastinal mass. The thoracic surgeon did not wish to proceed with resection of the primary tumor and a Wookey type of reconstruction unless he could be certain that the questionable mass was not due to metastatic tumor.

Angiocardiographic study showed conclusively that the abnormal shadow above the aortic arch was a large vessel arising from the aorta — presumably an aberrant right subclavian artery.

Angiocardiographic examination in this case provided additional evidence to encourage a definitive surgical procedure. Resection of the tumor was performed, and the opinion of the roentgenologist confirmed.

DISCUSSION

The wide variation in the clinical appearance of the cases discussed is representative of some of the situations discovered in the mediastinum. The importance of survey roentgenographic examination in the detection of mediastinal lesions cannot be questioned, but identification of these lesions requires complex procedures. In many of the patients there was little clinical evidence to help decide whether thoracotomy should be done. Before the advent of modern angiocardiography most of these patients would have been handled in stereotyped fashion, a thoracotomy being performed for each of the "mass" lesions discovered. Thus, the patients with the pulmonary-artery aneurysm, the absent left pulmonary artery, the dilated aberrant right subclavian artery lying between the esophagus and aorta, the coarctation of the aorta and the pulmonary veins emptying into the superior vena cava might all have been unnecessarily subjected to the discomfort and danger of thoracotomy.

In none of these cases could any definitive surgical procedure have been carried out successfully, with the possible exception of the woman with coarctation of the aorta (Case 6). Moreover, the abnormal vascular structures might have been seriously damaged if such a procedure had been performed blindly — that is, without angiocardiography. Establishing the true nature of the questioned shadows eliminated any need for further procedure at the time.

On the other hand, in Case 9, the determination that the shadow adjacent to the aorta represented a part of the cardiovascular system and not a metastatic lesion strengthened the indications for surgical intervention, thus influencing decisively the plan of treatment.

In the cases of hypertrophic lymph nodes adjacent to the left side of the heart near the pulmonary artery, of the (as yet) unidentified mass above the aortic arch and of the enlarged thymus in the little girl, the angiocardiographic demonstration that the abnormal shadows were not cast by integral parts of the vascular system was of great clinical significance. Two of these patients were subjected to definitive surgery, and the third probably will be if her mental state improves.

This method of study is undoubtedly of enormous value, both positive and negative; it strengthens the case for mediastinal exploration in some patients and in others establishes the fact that thoracotomy is unnecessary and possibly dangerous.

SUMMARY

Mediastinal masses, frequently asymptomatic, present a challenging diagnostic and therapeutic problem.

Angiocardiography, by disclosing the vascular or nonvascular nature of a mediastinal lesion, can decide the question whether or not mediastinal exploration should be performed.

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EMBOLIZATION IN THE SURGERY OF MITRAL STENOSIS*

Report of a Successful Aortic Saddle Embolectomy

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AS the result of increasingly frequent surgical procedures on the heart for acquired valvular disease, a significant number of cases of peripheral embolization have occurred either during or shortly after operation. Specifically, this complication has been reported with surgery for mitral stenosis,[1-3] the source of the emboli being either the clots occasionally present in the enlarged fibrillating left atrium or the calcium deposits on the diseased valve leaflets. In addition, operative technics designed to prevent fatal cerebral emboli during intracardiac manipulation have resulted in emboli of major or minor import in the distal vasculature.[4] The latter situation is considered desirable, for adequate treatment is more feasible and prognosis is greatly improved. One of the potentially most disastrous embolic sites is the aortic bifurcation, since an untreated saddle embolus carries a mortality of about 75 per cent.[5] Fewer than 60 successful aortic embolectomies have been reported in the literature.[1] In the past the outlook for this disease, even with adequate surgery, has not been favorable because of the underlying cardiac disease.

Although such emboli occur with myocardial infarction and with atrial fibrillation from any cause, the most common cause is rheumatic heart disease with mitral stenosis. From the long-term point of view, it is becoming evident that the prevalence of emboli after adequate surgery for mitral stenosis is apparently decreasing. Furthermore, these patients have been shown to be better operative risks than they were before commissurotomy.[6]

From the short-term point of view the outlook for embolus occurring during or immediately after mitral-valve surgery appears to be better for several reasons. These patients are in the hospital and the factor of delay between occurrence and removal of the embolus is at the theoretical minimum. This minimal delay can be achieved by an increased awareness of the problem by all attending personnel, resulting in prompter recognition. It is becoming a matter of record that the patient, in the early period after commissurotomy, can tolerate further emergency surgical intervention.[6] Because of the generally younger age group there are certain innate technical advantages to the embolectomy itself.

In light of these considerations the management of patients undergoing mitral-valve surgery must include measures for the prompt recognition and treatment of possible peripheral emboli. Two recent cases of aortic saddle embolus occurring with commissurotomy furnish the impetus for this report. They serve to point out some unusual features of the problem as well as to emphasize the routine measures that are necessary for a successful outcome.

CASE REPORTS

CASE 1. E.M., a 35-year-old housewife, was admitted to St. Elizabeth's Hospital on April 27, 1953, with a chief complaint of increasing dyspnea.

She had had frequent "sore throats" with high fever in childhood but had remained in relatively good health until 8 years before admission, when she noted gradual onset of dyspnea. There was no history of rheumatic fever. Approximately 3 years previously the dyspnea had become worse, and since that time she had required digitalis, ammonium chloride and injections of mercurial diuretics. In December, 1952, she was hospitalized elsewhere for treatment of cardiac decompensation. During this admission there was an episode of unconsciousness that lasted for 7 days, had no ready explanation and left no apparent, neurologic residua. During the past 4 months she had had orthopnea requiring 3 or 4 pillows. Review of the systems was negative except for anorexia of several months' duration.

Physical examination revealed a thin woman sitting up in bed and appearing dyspneic and chronically ill. The trachea was in the midline. Expansion of the chest was equal, and the lungs were clear to percussion and auscultation. There were no thrills. The heart was enlarged to percussion. A Grade 2 mid-diastolic murmur was heard at the apex. The pulmonic 2d sound was accentuated, had a snapping quality and was louder than the aortic. The heart rate was 120, with a grossly irregular rhythm, and the radial pulse rate was 84. The blood pressure was 130/80. Respirations were 30, and the temperature 97.8°F. The liver edge was palpable 4 cm. below the right costal margin. There was a 1-cm. decubitus ulcer on the buttock. There was slight ankle edema. Pulses in the lower extremities were noted but difficult to obtain. The remainder of the physical examination was within normal limits.

Examination of the blood showed an elevation of hemoglobin (16.2 gm. per 100 cc.) and hematocrit (50 per cent). The white-cell count was 7200, with a normal differential. The fasting blood sugar, nonprotein nitrogen and prothrombin time were within normal limits. The urine contained a trace of albumin.

Roentgenographic study disclosed enlargement of the heart involving principally the left atrium and right ventricle. The esophagus was displaced by the enlarged left atrium, and the hilar vessels were prominent. The lung fields were clear. The findings were interpreted as being consistent with mitral stenosis. An electrocardiogram was interpreted as showing coarse atrial fibrillation and right-axis deviation.

The patient was prepared for operation. The disease was considered to be Class IV according to the classification of the New York Heart Association.

On May 1, a mitral commissurotomy was performed by one of us (I.M.M.). At operation a firm clot, 2 by 3 cm., was obtained from the left atrium during flushing before the

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examining finger was inserted. A satisfactory commissurotomy was performed, by the finger-fracture technic, the valve orifice having been enlarged from less than 0.5 to 3 cm. No calcification or regurgitant jet was noted. Bouts of tachycardia and cyanosis, which occurred at the time of intracardiac manipulation, ceased afterward.

When the procedure had been completed the patient's peripheral pulses were palpated with difficulty; the blood pressure was depressed. On awakening the patient noted that her feet were cold, but physical examination revealed no change from the previous status. Sixteen hours after operation she said that her feet were warm. Four hours later increasing dyspnea was noted. Physical examination showed findings consistent with partial atelectasis of the left lung. Tracheal suction was performed, and the thoracic drainage tube was removed. At the completion of these procedures she felt greatly improved and was no longer dyspneic.

On the 2d postoperative day she walked around her bed without difficulty. As the day progressed she became increasingly apprehensive. The respiratory rate rose slowly from 20 to 40 per minute. Several hours later she started to note some numbness in both legs, but the temperature and color of the legs showed no remarkable change. The lung fields remained clear. Dyspnea increased, and all extremities became somewhat more cyanotic. Oscillometric examination of the legs revealed no oscillations. A diagnosis of saddle embolus of the aorta was made and preparations for emergency operation were started. In this period, the patient became increasingly dyspneic, and pulmonary edema developed. Control measures were of no avail, and she died 70 hours after operation.

Autopsy demonstrated a fresh, laminated clot in the aorta extending from a level below the renal arteries to the aortic bifurcation and into each iliac artery for a distance of 1 or 2 cm. The right main pulmonary artery was completely occluded by an old, gray-white, laminated thrombus. There was pulmonary congestion and edema. The mitral-valve orifice was found to have been satisfactorily opened through the previously fused edges. There was chronic passive congestion of the liver, spleen and kidney.

It is believed that the initial phase of saddle embolization may have occurred at the time of or shortly after operation. However, in view of the clinical progress, complete occlusion must have occurred at some subsequent period. At no time during the early postoperative course were the findings sufficient to justify a diagnosis of embolism. Oscillometric examination was carried out when the patient complained of numbness. The thrombus occluding the right pulmonary artery was quite old and organized; this may have occurred during the hospitalization four months before admission. Its presence undoubtedly contributed to the bouts of tachycardia and cyanosis occurring during cardiac manipulation at operation when the left lung was partially collapsed. The diminished functioning pulmonary reserve attendant on this thrombus may well have contributed to the extremely rapid course after she began to have difficulties as the result of the saddle embolus.

Case 2. J.E., a 43-year-old housewife, was admitted to the Massachusetts Memorial Hospitals on July 8, 1953, with a chief complaint of increasing exertional dyspnea.

The patient had had Sydenham's chorea at 7 years of age, with persistence of symptoms for 12 years thereafter. During the 10 years before admission she had hemoptysis on several occasions, starting with a pregnancy, when digitalization was required. There were increasing exertional dyspnea and several episodes of paroxysmal nocturnal dyspnea. Four months before admission, she started to have a cough, with expectoration of blood-tinged sputum; ankle edema was recently noted. She was followed in the Outpatient Department. She was admitted to the Medical Service of the hospital with atrial fibrillation and congestive cardiac failure. On a course of quinidine the fibrillation reverted to regular rhythm. On the 6th hospital day she was found to have thrombophlebitis of the right leg; she was treated with heparin and Dicumarol, and the phlebitis subsided within 3 days. She was transferred to the Thoracic Surgical Service for mitral-valve surgery with a diagnosis of rheumatic heart disease and mitral stenosis.

A review of the past history and of the systems revealed that she had epilepsy, grand-mal type, which was very satisfactorily controlled with Mesantoin. There was conductive deafness on the left that had followed mastoidectomy 7 years previously.

Physical examination showed a thin, anemic, chronically ill woman. The neck veins were somewhat distended. The trachea was in the midline. Expansion of the chest was equal. There were some fine rales at both lung bases posteriorly. The heart was enlarged to percussion. There were no thrills. A diastolic murmur with presystolic accentuation was heard at the apex. The pulmonic 2d sound was accentuated. The rhythm was regular, at a rate of 70. The blood pressure was 120/70. The liver edge was palpable 2 cm. below the right costal margin. Examination of the peripheral circulation revealed that the right foot was somewhat cooler than the left. All peripheral pulses were easily palpable, except those in the right dorsalis-pedis and right posterior-tibial arteries.

Examination of the blood demonstrated a red-cell count of 4,210,000, with a hemoglobin of 9.9 gm. per 100 cc. and a hematocrit of 33 per cent, and a white-cell count of 7450, with a normal differential. The non-protein nitrogen and fasting blood sugar were within normal limits. The urine had a specific gravity of 1.017 and contained a trace of albumin.

Roentgenographic study showed the heart to be enlarged. The pulmonary artery was prominent. The left atrium was enlarged, and the barium-filled esophagus displaced. The lung fields revealed prominent hilar shadows, with increased intensity of the pulmonary markings. An electrocardiogram indicated right-axis deviation and regular sinus rhythm.

The patient was prepared for operation. The anemia was treated by infusion of packed red blood cells, and the hemoglobin thus corrected to 13.8 gm. per 100 cc. The disease was considered to be Class IV, according to the classification of the New York Heart Association.

On the morning of July 31, mitral commissurotomy was performed by one of us (J.W.S.). At operation, a thrombus, 3 by 1 cm., was extracted from the atrium. A satisfactory commissurotomy was achieved by the finger-fracture technic. The valve orifice was opened from a size equivalent to the tip of the finger to 2 fingers. No regurgitant jet or calcification was present.

At the completion of the procedure the patient's general condition was good, with stable blood-pressure readings. The peripheral pulses were the same as they had been before operation. Her condition remained quite satisfactory during the early postoperative period. At 2 p.m. on the afternoon of the 1st day she was bright and co-operative. A routine examination of the peripheral pulses revealed no change from the preoperative status. Two hours later she began to become progressively more drowsy. The lower limbs were slightly cooler than previously, but their color was excellent. At this time the arterial pulsations distal to the femoral vessels could not be palpated; the femoral pulsations became weaker and disappeared completely within 1 hour. The radial pulses and blood pressure remained stable. Oscillometric examination of the lower extremities was carried out, confirming the absence of femoral-artery circulation. The patient's drowsiness increased.

A diagnosis of saddle embolus of the aorta was made, and embolectomy was done by 2 of us (J.E.T. and I.M.M.) within 3 hours through a left paramedian incision. A saddle embolus was found in the distal aorta extending into both common iliac arteries for a distance of 2 cm. After the aorta and both iliac arteries proximal and distal to the embolus had been occluded with No. 10 rubber catheters, the right common iliac artery was incised, and the embolus was removed. The portion in the left common iliac artery was

easily mobilized into the lower aorta and then extruded through the same incision. The arterial incision was closed with a continuous, No. 0000 silk suture after flushing of blood from the aorta through the incision. Pulsations distal to the previous points of occlusion became palpable immediately.

Postoperatively, the patient's general condition was good. On the following morning femoral pulsations were palpable, and the feet were warm and of good color. The peripheral circulation, which was observed with oscillometric examination from time to time, showed good improvement. On the 2d postoperative day, intravenous administration of heparin was started. The postoperative course remained satisfactory. On the 10th postoperative day progressive ambulation was started. Exercise tolerance was greatly improved. The peripheral circulation was excellent, all pulses being easily palpable on the 4th day after embolectomy. She was discharged on the 21st day after commissurotomy.

Discussion

It is evident from the foregoing cases that the successful management of patients with peripheral emboli developing during or shortly after surgery for acquired valvular disease depends primarily on prompt recognition and treatment. To await the appearance of the usual characteristic symptoms of arterial occlusion is not sufficient. In Case 1 the patient became increasingly apprehensive and gradually dyspneic, without change in pulmonary signs. The patient in Case 2 became progressively more drowsy. Only after these general changes occurred was attention called to the local situation in the extremities. In Case 1 the patient complained of numbness in the feet, and in Case 2 the patient had no complaints, but the extremities were cooler than before, and the peripheral pulses had disappeared. The majority of patients sustaining an aortic saddle embolus have severe leg pain, which progresses to numbness and paralysis. The pain, however, may be in the abdomen, low back or gluteal region, rather than in the legs and may, in fact, not be present at all. One must emphasize here the importance of objective criteria in diagnosis, especially in patients whose sensoriums may be dulled as a result of anesthetic agents or analgesic drugs.

The house and nursing staffs must be carefully indoctrinated in the problem of arterial embolization in these patients at any time during their hospital stay. In the preoperative work-up all the peripheral pulses, including the axillary, brachial, radial, ulnar, femoral, popliteal, posterior tibial, anterior tibial and dorsalis pedis, should be searched for and recorded in the chart as normal, reduced or absent. The exact location of any pulse that is difficult to palpate should be marked on the patient's skin with indelible ink to facilitate rapid checking. If pulses are absent or equivocal oscillometric examination should be carried out. In addition the determination of collateral circulation time[7] gives valuable information and is easily accomplished as follows: if, after blanching on elevation, there is flushing in the tips of the toes within twenty seconds or less, or if there is filling of the veins on the dorsum of the feet within thirty seconds or less, the collateral circulation is considered to be adequate.

During the cardiac operation several important precautionary maneuvers must be carried out. When the atrium is opened and before the finger is inserted, blood should be allowed to gush forth briefly to flush out any loose thrombi. Occasionally, when the finger is inserted into the atrium, loosely attached or free clots may be felt that can be removed by repetition of the flushing procedure before valve manipulation. One attempts to prevent cerebral emboli during commissurotomy by intermittent occlusion of the innominate and left carotid arteries by means of tapes. Occlusion for thirty-second intervals can be repeated as often as required for accomplishment of a satisfactory commissurotomy.

Immediately after operation — before the patient has left the operating table — the peripheral pulses are carefully re-examined. If there is evidence of major peripheral embolization, decision about embolectomy can be made at this time. From this time forward, the status of the peripheral pulses is determined and recorded at hourly intervals for forty-eight hours. This can be done easily and quickly by nurses as well as house officers since the location of the pulses has previously been established. Any change in the status of the peripheral pulses calls for a prompt general as well as local evaluation to determine the occurrence of embolic phenomena. As a corollary in the light of the 2 cases herein reported any change in the general status of the patient calls for an immediate, complete examination, including peripheral pulses. Oscillometry and determination of collateral circulation times are also carried out.

Once the diagnosis of major peripheral embolus has been made, embolectomy is the treatment of choice for aortic, iliac and femoral emboli. To be successful, embolectomy must be carried out early — at most, eight to ten hours after its occurrence. Despite the fact that a patient has recently had mitral-valve surgery, his general condition will usually permit removal of an aortic saddle embolus. Saddle embolectomy is unquestionably best carried out by a transabdominal approach. In this way the embolus can be satisfactorily removed through an incision in one common iliac artery. The clot in the aorta and the other iliac vessel can be milked out through a single arteriotomy wound. Soft-rubber catheters or non-crushing clamps are used to prevent the passing of emboli into the distal vasculature and to control bleeding. If the patient is too ill for a transabdominal maneuver, the bilateral femoral approach under local anesthesia can be utilized. This may be attended by success, but it is less satisfactory technically than the direct aortic approach.

Certain adjuncts are of value in the management of patients with peripheral emboli. These stem from the events that follow the mechanical obstruction, including spasm of the main and collateral arterial

vessels and secondary thrombosis both proximal and distal to the embolus. Vasospasm may be relieved before embolectomy by paravertebral sympathetic procaine block or spinal anesthesia. If the lumbar sympathetic trunks are readily accessible at the time of embolectomy, simple division of the trunks or removal of single ganglions may be done. Otherwise, paravertebral blocks can be done twice daily after embolectomy if necessary, due attention being paid to any anticoagulant therapy.

Secondary thrombosis is best prevented by the use of anticoagulants. Heparin can usually be safely instituted six to eight hours postoperatively and continued for as long as indicated. One should be alert to the possibility of intrathoracic bleeding as a result of anticoagulant therapy. Finally, the head of the patient's bed should be placed on blocks 10 to 15 cm. high to ensure dependency of the legs.

Embolism associated with mitral-valve surgery occurs relatively infrequently but it is the most significant immediate danger attending operation. However, the risk must be viewed in the light of the possibility of embolism without operation, the continued disability as the result of untreated mitral stenosis and the diminished likelihood of embolism after successful surgery. Intra-atrial clot may be removed by cardiotomy without resulting in peripheral embolism. One need not dwell on the inadequacy of removal of the atrial appendage alone for this purpose. Since one can prevent cerebral embolism during surgery by directing the clot to the peripheral vasculature, peripheral embolism should not affect the ultimate prognosis if management is adequate. The comprehensive surgical care of the patient with mitral stenosis must include provisions for prompt recognition and treatment of peripheral emboli.

Summary and Conclusions

Peripheral embolism occurring at any time during hospitalization for mitral-valve surgery can be effectively treated. The basic factor in success depends on an alert awareness of the problem accompanied by a standard routine of examination.

The management of these patients is reviewed.

Two cases of aortic saddle embolism after mitral-valve surgery are reported. In 1 of these, successful aortic embolectomy was accomplished thirty-four hours after mitral commissurotomy.

Attention is called to the unusual general symptoms of these patients.

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USE OF SUGGESTION IN PSYCHOTHERAPY

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IT is generally conceded that suggestion can powerfully influence thinking, either for good or for ill. Every physician knows that throughout history various medications and types of treatment that could only have helped by means of suggestion, have brought about amelioration or cure of different disturbances, and that many patients become emotionally disturbed as a result of unfortunate suggestions that cause worry and tension. Often such suggestions are made by physicians themselves; therefore, they must constantly be on guard to avoid causing unnecessary fears. For instance, if a physician listens long to a patient's heart or chest and says nothing, or even if he says that everything is all right, the patient may become apprehensive.

Before the flowering of psychoanalysis, practically all psychotherapists intentionally made use of suggestion, often with excellent results, and there is no doubt that suggestion plays a part in all psychotherapy, whether or not it is used intentionally. Even though a physician may listen in silence to a patient's account of his difficulties and say nothing, suggestion will probably take place because that patient will almost surely be mindful of what he suspects the physician is thinking; this may affect him just as much as though something had actually been said. If a patient discusses tentative plans about which he has conflicting feelings, he may know or think he knows the physician's opinion of the plans, even though that physician says little about his opinion. What the patient believes the physician is thinking will in itself influence him.

If a patient relates to a psychiatrist all his upsetting past experiences he does so with the hope that this will be helpful; therefore he will be influenced by the suggestion of anticipated benefit. When a particular

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type of psychotherapy has seemed helpful, it is difficult to tell whether the benefit has been due to suggestion, the understanding and education derived by the patient, the duration of therapy or some other circumstance.

Since the goal of psychotherapy is the modification or change of attitudes and reaction patterns and since suggestion enters into all psychotherapy, it seems sensible for psychotherapists to use suggestion intentionally, concerning themselves with the best methods of applying it, but it is fair to say that in these times most psychiatrists do not make much intentional use of suggestion. In recent years this technic has been regarded by many as a superficial and inferior method. This is undoubtedly true if the purpose of the therapy is solely to relieve symptoms such as indigestion, sleeplessness and fatigue. However, if suggestion is employed to help patients become better adjusted it is as fundamentally oriented as any other type of psychotherapy because its object is to teach people to react differently and to be controlled by constructive attitudes.

For a change of attitudes to take place, there are two requirements: the patient must be strongly motivated to react differently, and he must be able to see clearly in what way he can act and behave differently —what different attitudes and behavior will lead to happier consequences.

A person may become strongly motivated to change as a result of reviewing his life, and in that way becoming acutely aware of how certain attitudes and behavior have led to uphappy results, but he may not clearly understand what positive attitudes and behavior he needs to develop to be happier and more effective. Many patients see what they want to get over but are not clear about what they need to focus on and work toward. By tactful suggestion a person can be helped to an appropriate goal, and by suggestion he can be stimulated to work persistently toward it; without the use of suggestion he may stumble and flounder before he finds his way, or he may never have goals that make a good adjustment possible. Thus, suggestion can greatly expedite psychotherapy and may ensure its success.

An effective way of using suggestion is the technic called "suggestion in relaxation." The patient is asked to relax on a couch or in an armchair. In attempting to secure a state of relaxation, the physician may bring about a state of light hypnosis, but this is not necessary and does not seem desirable. With the patient at ease and not attempting to answer or listen, the physician reviews and emphasizes what has already been discussed with and accepted by him—subjects having to do with an understanding of the psychologic causes of his upset state and with different attitudes and patterns of reaction that will make for a better life and more abundant health. It is essential that the suggestions given be positive in character, and that they be directed toward helping the patient to retain the attitudes and spirit by which the results desired will be achieved. Thus, in the case of a stammerer, such suggestions as "You will not stammer" are negative and should be avoided and such suggestions as "You will talk well," though positive, are not particularly helpful because they do not bring out the means by which this is to be achieved. However, certain suggestions ("You will take pride in reacting well; you know that people will respect you more if you react well to speech difficulty than if you do not have any difficulty at all. You will be completely absorbed in what is going on, and you will feel at ease with others —if you have trouble you will relax and start over") point out attitudes that promote freedom from tension and, consequently, better speech.

The suggestion should be given that each morning the patient will get set to express the attitudes he wants to develop, by going over them in his mind and by picturing himself expressing them. Unless a patient works day by day to strengthen attitudes that need strengthening he may not make progress.

The following suggestions were given to a man who had paranoid ideas that his fellow workers did not like him or think well of him:

> You're going to train yourself to be objective—to focus on the thing, and also to express team feeling yourself, no matter what others do or don't do. As you express team feeling it will become stronger and stronger in you. You'll make others feel that you have it by the way you look at them, by the way you smile, by the way you laugh with them. You know that team feeling gives great satisfaction —it makes for good relationships between people. It makes for good relationships in work. You'll look forward to each day as an opportunity for expressing it and as an opportunity for expressing dedication to your work.

A woman, who was upset because attitudes and behavior of her husband created difficulties, received the following suggestions on several occasions:

> You will face your problems squarely. You will keep thinking in terms of what to do about them—of what action to take. You'll nip resentment or hostility in the bud so that you won't dwell on it. If there isn't anything to do about a problem you will turn your mind to other things—to things that give you satisfaction and that help you to compensate. You know that things can't upset you if you take them well—if you think purposefully about them—in terms of what to do—of what the next step is. You will get set each day to react well—to do what there is to do.

To a patient with a mild cyclothymic depression, the following suggestions were repeatedly given:

> You understand that the upset state you are in is like a storm. It blows over after a while. The body is made so that it cures itself. These conditions get well after a time. No matter how badly you feel, you will be confident and patient. Nothing will shake your confidence that you will get well, and then everything will seem all right again.

Suggestions are given at the end of an interview so that the patients will not be distracted from them by subsequent discussions. Most of each interview is given over to the patient's account of how he has been feeling, the difficulties and upsetting experiences he has had and his reactions to them. In succeeding

sessions new developments occur that call for different suggestions, so that the focus often changes as therapy continues. In this way the patient can be helped to react more constructively to the various problems that he encounters, and he can be helped to outgrow personality traits that cause difficulties in human relations. It is important to avoid forcing unacceptable suggestions on the patient. Only when the suggestions fill a need will they be beneficial.

For suggestions to be fundamentally oriented, it is first necessary to learn what ideas, attitudes, feelings and patterns of reaction have caused difficulty in adjustment. Therefore, a detailed history is taken with a review of the patient's past before any suggestions are given. The patient is encouraged to talk freely, and both he and his physician discuss the feelings, attitudes and reactions that have caused difficulty. Several interviews may be necessary before the physician believes that he understands the case well enough to direct suggestions intelligently and helpfully and before he decides that the patient is ready to accept them. When physician and patient are ready, the former explains that he wants to help the latter by a different method, describing what he proposes to do and why. Suggestions given in relaxation do not replace technics such as ventilation, discussion and explanation of conventional psychotherapy, but add to the benefits of usual technics by crystallizing and emphasizing important points and helping the patient to attitudes and a spirit and a philosophy that make for a better adjustment.

The level of the intelligence of the patient seems to have little effect on the result. The important determinant is that the suggestions are accepted by the patient. Discussion beforehand will indicate what the patient will accept.

This technic has the advantage of not being protracted. After the attitudes and patterns of reaction causing trouble and the attitudes that need to be strengthened have been understood, a visit of half an hour, one to three times a week, is sufficient, and as the patient improves, the intervals between visits are longer. Because the technic is simple and not time consuming, it is adaptable to the use of physicians who are not psychiatrists. A surgeon can employ it to help a patient to take an operation well, and an internist can use it in connection with various problems. It is of particular use in the management of depression and anxiety. It has proved helpful to record the suggestions given and to send them to the patient so that he can work on them day by day.

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ACUTE LEUKEMIA WITH RUPTURE OF THE SPLEEN AS THE INITIAL SYMPTOM*

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SPONTANEOUS rupture of the spleen has been reported in many diseases associated with splenomegaly. Malaria, the most common of these, was found in 50 per cent of 44 cases of spontaneous splenic rupture seen in the Army Institute of Pathology.[1] Infectious mononucleosis, the second most common associated disorder, was present in 7 cases. Other diseases in which spontaneous rupture of the spleen has been reported include tularemia,[2] sarcoidosis[3] and infectious hepatitis[4] although the last case may have been one of infectious mononucleosis with hepatic involvement.

In leukemia splenic rupture is rare. Lange[5] observed leukemia in only 5 of 189 cases of spontaneous rupture. Only a handful of cases are reported in the literature.[6-11] In most of these the leukemia was acute; in 1 case,[10] in which the patient died at birth from rupture of the spleen, some of the reviewing hematologists considered erythroblastosis the most likely diagnosis.

The case reported below is one of authenticated, acute leukemia. The patient was completely symptom free until spontaneous rupture of the spleen occurred.

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CASE REPORT

A 59-year-old printer was admitted to the hospital on October 28, 1952, for the first time. On the morning of admission, while at work, he had reached for an object with his left hand. At that time severe pain in the left upper quadrant of the abdomen suddenly developed, increasing with respiration and radiating up the left side of the chest and to the left scapula. This pain was followed by nausea, vomiting and sweating. He had noted no unusual symptoms the past few weeks and, on repeated, direct questioning, denied any recent sore throat, lymphadenopathy, rash, headache or malaise.

Except for a duodenal ulcer and an episode of jaundice in 1918, the past history was irrelevant.

Physical examination revealed a stocky, well developed man with a pale, cool and clammy skin. The abdomen was slightly distended, without rigidity. There was moderate epigastric and left-upper-quadrant tenderness. The prostate was minimally enlarged. Slightly enlarged, nontender cervical lymph nodes and 1 moderately enlarged femoral lymph node were observed on the left. The remainder of the physical examination was negative.

The blood pressure was 76/50 in both arms. The temperature was 99° F., the pulse 120, and the respirations 24.

The results of repeated blood studies are presented in Table 1.

Urinalysis revealed a maximum specific gravity of 1.021 on routine specimens. A slight to heavy trace of albumin was present consistently, and the sediment contained 20 to 25 white cells, 3 to 5 red cells and 3 to 5 coarse, granular casts per high-power field. The fasting blood sugar was 138 and 129 mg. per 100 cc. The nonprotein nitrogen was 50 mg. per 100 cc., rising to 75 mg. and subsequently dropping to 44 mg. per 100 cc. A blood Hinton test was

negative, and bleeding, clotting and prothrombin times and serum amylase and electrolytes were normal. An x-ray film of the chest, a plain film of the abdomen and an electrocardiogram disclosed no abnormalities.

Aspiration biopsy of the iliac crest revealed lymphocytosis and erythroid hyperplasia of the marrow. On biopsy of a femoral lymph node on the left the tissues showed extensive infiltration of the sinusoids and the reticulum by cells of the lymphoid series, most of them being adult types of lymphocytes, and some of them being less mature but not characteristically lymphoblastic; no basic architectural destruction was present, however.

The patient was in shock on admission and he received a transfusion of 2 pints of blood. Twelve hours later the blood pressure had stabilized at 120/80. On the 2d hospital day his condition was greatly improved. He had very little pain, but the abdomen was distended and silent. There was slight tenderness over the left upper quadrant and rebound tenderness referred to the left upper quadrant from the remainder of the abdomen. A great increase in splenic dullness was found, and on the following day, shifting dullness in the abdomen was elicited. At no time was any spasm observed.

During the first 3 days severe oliguria was present, and surgery was withheld and the patient observed closely until this was corrected. Since the red-cell count and hemoglobin continued to drop operation was performed on the 4th hospital day. The preoperative diagnosis was rupture of the spleen, possibly secondary to infectious mononucleosis.

At operation massive hemoperitoneum was found. The spleen was about 3 times the normal size and had ruptured tangentially along its posterior fourth. The organ was removed without incident.

The patient did well postoperatively. However, on the 10th day generalized lymphadenopathy appeared, and about this time the positive heterophil-antibody agglutination was found. Adsorption studies with guinea-pig kidney were not done. The patient was discharged on the 18th day, when the adenopathy was still present.

Microscopical examination of the spleen showed the same general findings that had been observed in the lymph-node biopsy: infiltration, without destruction, by lymphocytes of both mature and immature types.

After discharge the patient felt well for a few days, but anorexia, vomiting, pruritus and frequent epistaxes developed. He began to lose weight and noted some skin ecchymoses, dark urine and light stools. Two weeks after discharge, a follow-up examination showed the liver to be enlarged to the right iliac crest. The white-cell count was 91,000 with 95 per cent small mononuclear cells. He was therefore readmitted to the hospital on December 4, 1952, for further observation.

Physical examination revealed the tremendous hepatomegaly described above. The liver was firm and smooth and minimally tender. There were scattered ecchymoses and numerous purpuric lesions throughout, especially on the legs. Moderate icterus was present. Several moderately enlarged, freely movable and nontender lymph nodes were observed in both cervical chains as well as in the right axilla.

Examination of the blood disclosed a red-cell count of 3,630,000, with a hemoglobin of 75 per cent (Haden–Hauser), and a white-cell count of 89,000, with 90 per cent lymphocytes. Platelets numbered 88,000. Heterophil-antibody agglutination was negative. The reticulocyte count was 4.1 per cent. The urine gave a positive test for bile, and the urobilinogen was 1:50. The nonprotein nitrogen was 50 mg. per 100 cc. The icteric index was 40. A stool gave a ++++ test for occult blood.

Aspiration biopsy of the bone marrow revealed almost total replacement of the erythroid and myeloid elements by mature, immature and blastic lymphocytes. The diagnosis was acute lymphatic leukemia. Lymph-node biopsy of the right axilla also demonstrated a lymphocytic lymphoma consistent with acute leukemia.

TABLE 1. *Results of Blood Studies.*

DATE	RED-CELL COUNT	HEMOGLOBIN (HADEN–HAUSER)	WHITE-CELL COUNT	NEUTROPHILS	MONOCYTES	LYMPHOCYTES	HETEROPHIL-ANTIBODY TEST	PLATELETS
	$x10^6$	%	$x10^3$	%	%			$x10^3$
Oct. 28	3.76	71	51.3	20	2	68	Negative	160.0
Oct. 29	3.36	68	59.8	26		74		
Oct. 30*	2.84	58	37.1	40		60		
Oct. 31†		62	8.5	35		65		
Nov. 1	3.59	71	7.6	54		44		
Nov. 3	3.74	75	6.5	66	1	32		280.0
Nov. 6	3.49	71	6.6	52		47		
Nov. 8	4.23	81					1:120	

*Reticulocyte count on this day 4.2 per cent.
†Operation on this day, after blood count.

The patient did poorly during this admission. Anorexia, vomiting and bleeding tendency persisted, with persistent jaundice and hepatomegaly in spite of transfusions. He died suddenly 8 days after admission.

Autopsy revealed extensive replacement and destruction of tissue by the lymphoblastic process in the liver, both kidneys and adrenal glands and all lymph nodes.

DISCUSSION

This case illustrates the importance of searching for the underlying lesion in any case of splenic rupture in which major trauma has not occurred. Careful hematologic work-up is indicated in these cases. The possibility of an underlying infectious mononucleosis is well recognized; less frequently considered are the more serious blood dyscrasias, which may also cause splenic rupture.

At times the differential diagnosis between infectious mononucleosis and leukemia may be difficult. Reliance on heterophil-antibody agglutination may lead to error, for a positive reaction may be obtained in leukemia unless the test includes absorption with guinea-pig kidney. Numerous workers[12-16] have described high agglutinations—up to 1:16, 384—in leukemia as well as in other diseases. Southam and his associates[17] reported 2 cases of acute leukemia in which the initial diagnosis of infectious mononucleosis was made because of a positive heterophil-antibody agglutination. They studied 94 patients with acute leukemia and found that 19 per cent had titers of 1:112 or more. In every case the antibody giving the

false-positive reaction was satisfactorily absorbed by guinea-pig kidney. It may therefore be concluded that only with absorption technics is a positive heterophil-antibody agglutination diagnostic of infectious mononucleosis; otherwise, a positive test is of doubtful significance, and may be misleading.

Another cause of delayed diagnosis in this case was the return of the blood counts and differential to normal during the first admission, before the splenectomy was performed. Such a sudden and spontaneous hematologic remission seemed to militate against a diagnosis of leukemia. It should therefore be emphasized that a transient, spontaneous remission is not unknown in acute leukemia. In both cases reported by Southam and his associates,[17] hematologic remission was present at the time the "positive" heterophil-antibody agglutination was obtained.

Summary and Conclusions

A case of acute leukemia is described in which the presenting symptom was rupture of the spleen. This case emphasizes the necessity of searching for hematologic disorders in all cases of spontaneous rupture. Although infectious mononucleosis should be strongly considered, a more serious dyscrasia may be present. Some of the difficulties of the differential diagnosis of infectious mononucleosis and acute leukemia are discussed.

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MEDICAL PROGRESS

DIABETES MELLITUS (Concluded)

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BOSTON

Treatment

Physiologic difficulty in regulation of some diabetic patients with widely fluctuating blood sugar levels is sometimes called brittleness; it may actually be attributable to more than one mechanism.† It may, on the one hand, refer simply to a patient with a relatively stable carbohydrate metabolism for whom a type of insulin with unsuitable proportions of regular and long action has been prescribed. This attribute of insulin is more critical in the severer diabetes, and the result of the disharmony is an apparent lability of blood sugar. Although the convenient NPH insulin is suitable for 50 per cent of severer diabetes,[118] its fixed ratio of long to short action makes it unusable in the remainder,[119] in which its duration of action frequently falls short of the full twenty-four hours, very much as that of globin does.[120] To remedy this, mixtures of regular and protamine zinc insulin are required, but these cannot be varied with easy clinical predictability.[121]

On the other hand, brittleness may refer to true daily fluctuations in carbohydrate metabolism, and this phenomenon varies widely in degree among such patients. However, even in those with milder degrees, the use of an insulin with uneven action may critically potentiate such fluctuations. All types of insulin in current use (mixtures of protamine zinc and regular insulin, NPH and globin) have this defect.[120,122]

A new type of insulin has been developed in Denmark (Novo Laboratories) in an attempt to correct both sources of blood sugar lability. It is simply zinc insulin (2 mg. of zinc per 1000 units) rendered insoluble at pH 7.2 by substitution of an acetate for the usual phosphate buffer.[123] In this system, the larger the size of the insulin crystals, the longer and less intense the action. Thus, two basic types have been prepared, ultralente and semilente, with durations of

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†Other pertinent physiologic factors involved are described in the sections on glucagon, over-all carbohydrate metabolism and hormonal interrelations.

action of thirty and twelve hours. The former resembles protamine zinc and the latter regular insulin with somewhat longer duration and lesser intensity of action. One important advantage is that mixtures of these two exert their separate actions without modification. Thus, a third type called lente has been prepared simply by mixture of 70 per cent of ultralente and 30 per cent semilente.[124] This resembles NPH, with duration of action of twenty-four hours. Extensive trial abroad has shown that this type of insulin is also smoother and less fluctuant in action than the present-day intermediate varieties. For these reasons, it may prove to be superior in difficult cases in which insulins in current use have been inadequate.[124-127]

In the initial regulation of a new patient the newer (NPH, lente) types of insulin can be employed from the start. I have used a simplified system of regulation, the method of successive approximations, which is both safe and rapid. It can be applied equally well to reregulation after an acute illness.[128]

Paley[129] followed 186 consecutive cases of diabetes after initial insulin therapy and found that lipoatrophy from insulin developed in 55 per cent. Of these, half were severe or moderately severe in degree, and the average time of appearance of this complication was about two hundred and seventy days. Most important, there was a definite predisposition to this late skin lesion on the part of those who had localized swellings at the injection sites in the early weeks of treatment.[129] This suggests that the swelling, at present considered only an annoyance, may be worth preventing, by a shift to less allergenic preparations or the use of antihistaminics.

In a patient with insulin resistance (without detectable allergic basis) an anti-insulin factor was isolated from the gamma-globulin fraction of the serum.[130] This was active in neutralizing experiments even in dilutions of 4 per cent, which supports the validity of the observation.

Severe insulin allergy occurs occasionally, and the best therapy is the use of many times (two to seven) recrystallized insulin. This is not available in the United States. Dolger[131] has devised a simple method of heat treatment to solve this problem. The entire bottle is immersed in boiling water for thirty minutes. The allergic qualities are removed by this process, and insulin activity is decreased by only 15 per cent. He suggested that only regular insulin could be so treated.* Patients lose their sensitivity after three or four weeks of therapy with this modified product.

Psychologic Aspects of Therapy

With the latest modifications of insulin, 90 per cent of diabetic patients could be rendered normoglycemic, but a majority are not. This is due mainly to dietary infractions. To achieve ideal regulation, only a reasonable constancy of the diet is actually required. Consequently, the difficulty lies in the psychiatric importance of the eating urge that the physician is attempting to restrain and the personal emotional handicaps of the given patient. Stearns,[132] in a recent, detailed analysis, underlines the need for an individual psychologic handling of these patients to match in degree the physiologic efforts — the need for a positive and sympathetic approach rather than the primitive persuasion by threat of complications.[132] Goodman et al.[133] have used group psychiatric therapy for elderly patients in the interest of economy of psychiatric facilities. This is a practical compromise whose permanence has yet to be proved. Psychiatric evaluation of the adjustment to the disease should be considered early in the regulation of all children and adolescents before improper attitudes and reaction patterns have become fixed.

Insulin therapy may be complicated by emotional tensions, which may engender a variety of symptoms simulating hypoglycemia that may confuse the handling of the ambulatory patient. Musser, Lorenz and Derus[134] recently described 14 such patients, whose symptoms were proved to be due to involuntary hyperventilation. Reproduction of the symptoms through a simple rebreathing experiment reassured each patient and allayed anxieties. This is not an uncommon emotional impediment early in treatment.

Pregnancy and Diabetes

The occurrence of excessively large babies as long as thirty years before a clinical diagnosis of diabetes has led to more intensive study of carbohydrate metabolism in pregnancy. Even in the normal pregnancy there is an elevation and prolongation of the glucose tolerance test, which is still within normal limits. There is partial reversion within forty-eight hours, but complete return to the prepregnancy level may take six months.[135]

In the latter months of pregnancy two types of abnormalities may occur: either a lowered renal threshold or an abnormal glucose tolerance test (or both). Within forty-eight hours of delivery the test frequently reverts to normal. Because of this and to ascertain whether large babies are associated with diabetes in pregnancy, the state of the carbohydrate metabolism must be determined before delivery in such cases. Most of the studies, however, have been retrospective. Thus, it has been shown that diabetes later develops in 62 per cent of women giving birth to infants weighing over 10 pounds.[136] Or the occurrence of large babies or stillbirths is three times the normal rate during the years just before clinical diagnosis of diabetes,[136] and total fetal loss is 50 per cent greater even than that among known diabetic patients in that period.[137] Lately, glucose tolerance tests have been performed more closely to but still

*I have encountered a patient in whom generalized urticaria developed on lente (Lilly, 70/30 mixture) insulin. After similar modification by heat, this insulin could be tolerated without further symptoms, and it had the further advantage of being both nonallergic and long acting.

after delivery of oversized babies. Of those done within three years of delivery 31 per cent were abnormal,[138] as compared with 44 per cent of those done two days post partum.

The facts strongly suggest that these are women with a low reserve carbohydrate metabolism that is converted by the stress of pregnancy into mild diabetes with or without glycosuria. The term prediabetes as used at present is without meaning and is misleading. The tendency to revert to normal after delivery and the occurrence of an elevated renal threshold among 20 per cent of such patients even during pregnancy have been important impediments to diagnosis.[135,139]

Such case finding has important therapeutic implications for both mother and child. A glucose tolerance test should be performed early, preferably intravenously, and repeated in the last trimester if negative earlier in any pregnant woman with glycosuria, obesity or a history of previous intra-uterine death or of birth of an excessively large baby (over 9 pounds). In interpretation of glucose tolerance tests and their therapeutic implications, it is well to realize that obstetric difficulties are as great among those with partially as among those with fully abnormal glucose tolerance tests.

Fetal losses in diabetes continue to be reduced. It is agreed that the unfavorable maternal environment rather than any specific fetal defect is still the main cause of this problem.[140,141] The solution seems to be twofold: to correct the defects of the maternal environment and to remove the fetus from its influence as soon as possible.

In 80 per cent of patients the diabetes of the mother tends to become worse in the sixth or seventh month, sometimes suddenly and strikingly so, and without relation to the initial insulin dosage.[142] Ketosis, which may ensue unexpectedly under such circumstances and, even when mild, may be associated with a high fetal mortality, still occurs as an important (42 per cent[137] and 30 per cent[143] of total fetal loss) and the most preventable cause of fetal mortality. Careful medical management of the diabetes is obviously the answer to this problem. Toxemia has hitherto been considered important in this respect. Recent figures show only a slightly higher fetal mortality[140,-144] associated with toxemia, which, in addition, can be successfully handled by immediate termination of pregnancy.[145] The use of hormones for this type or any diabetic pregnancy has become more debatable as a result of success without them[145] and of a properly controlled study of this factor.[146] The presence of renal disease is an unfavorable factor not capable of modification, and its progression is justification for termination of pregnancy. The presence or absence of renal disease may be a better basis for prognostic classification than simple duration or age at onset of diabetes.[145]

Removal from the maternal environment before term is a valid recommendation. Intra-uterine death rates rise during the thirty-sixth week or earlier.[140,-141,144,145] Yet too early a removal from the uterus increases the newborn death rate inordinately in spite of the most advanced pediatric care. The present consensus favors compromise on delivery at the thirty-fifth to the thirty-sixth week. Induction and delivery from below at this earlier period substitutes a different hazard for the large and fragile fetus. Accordingly, the use of the cesarean section has increased to 33 to 75 per cent in different series utilizing earlier delivery. The decision is based on good obstetric judgment regarding each case. The time rather than the route of delivery is the vital factor. In an attempt to reduce this to a matter of delivering a mature and not a postmature child, x-ray determination of fetal epiphyseal age has been utilized as an objective test.[146] However, the results are not yet conclusive.

Pedowitz and Shlevin[145] have just reported a remarkably low mortality of 8.2 per cent in a series of 73 deliveries from 1950 to 1953. This is a reduction of 66 per cent from their previous experience and is attributable simply to the use of all the above principles. They believe that further improvement is possible.

Complications

Metabolic Acidosis

It is important to recognize that occult electrolyte losses exist unrecognized among diabetic patients as measured by serum magnesium[147] and total body potassium.[148] These constitute additional deficits with which diabetic patients may enter into acidosis.

Nabarro, Spencer and Stowers[149] have divided into three stages the repair of the metabolic deficits during the twelve days after start of therapy of diabetic acidosis. In the first stage, comprising the first two days, water balance is almost completely and electrolyte deficit only 40 per cent restored. In the second, from the second to the sixth day, inorganic potassium, magnesium and phosphate stores are restored by another 30 per cent while repletion of cellular glycogen and organic phosphate is still occurring. In the first two stages therapy by potassium can prevent undesirable migration of sodium into the cells provided excessive sodium is not administered. Protein restoration lags in this period because of starvation and hyperadrenocorticalism. With the correction of these factors, it proceeds more rapidly into the third stage (last six days) but may take weeks to be completed. The third stage also sees the correction of the final 30 per cent of electrolyte losses.

Further studies on the lactescent serums of diabetic acidosis have shown that the excess lipids (mainly neutral fat) that appear are loosely bound to the serum protein.[150,151]

Zieve and Hill[152,153] analyzed the clinical features of a large series (124 cases) of patients with diabetic acidosis, with emphasis on prognosis. There was a

threefold increase in deaths among new patients. This may have been due to a delay in therapy because of the added time required for diagnosis. The initial treatment was the same for all cases. Recognition of the seriousness of the ultimately fatal cases was frequently delayed, and this also postponed the necessary intensification of therapy. The authors advocated the early use of a prognostic index to correct this situation and proposed a new, improved index utilizing six weighted variables: associated condition, blood sugar, blood urea nitrogen, blood pressure, duration of coma and mental status.[153] Fatal cases were considered likely to result from cardiorenal decompensation.

With an aging population, accompanying complications offer an increasing handicap to recovery. Under such circumstances, only the best possible clinical management of the metabolic disturbances will suffice. In addition to recognized reasons for using scientifically conceived replacement solutions,[154,155] potassium lack may be harmful to the proper function of smooth muscle and may specifically potentiate gastric dilatation,[156,157] cardiovascular collapse and renal failure.[158,159] It is still essential to be critical in correlating clinical with biochemical abnormalities. For example, Henderson[160] has described an abnormal but reversible electrocardiographic pattern in 10 cases of diabetic acidosis: high-peaked T waves in the leads of the right and flat or inverted T waves in those of the left side of the chest. These findings, with relation to the serum potassium, correspond to those seen with both high and low levels. It is obvious that the explanation must be sought in other, more complex electrolyte disturbances. An example of this is the participation of the serum calcium level in the QT-interval abnormality as contrasted to any effect of hypopotassemia.[161] This re-emphasizes the need for meticulous use of proper repair solutions.

Recovery is measurably slow not only chemically but also physiologically. Bernstein et al.[162] utilized multiple renal-function tests to study the recovery of kidney function. In some patients the abnormal function was rapidly reversed. In 2 cases the reversal took two weeks and azotemia was present. Azotemia may represent reversible organic lesions and suggests the presence of the same process in other organs less amenable to such quantitative study.

A comparison has been made of the action of insulin by the intravenous and subcutaneous routes.[163] The former is more effective and prompt, but of shorter duration. This justifies the common practice of administering insulin intravenously at the onset of coma to ensure prompt action.

Fructose utilization is independent of insulin, and this sugar is therefore better utilized in replenishing the depleted liver glycogen in diabetes.[164,165] Early experiments on normal human subjects in the postoperative state showed decreased glycosuria because of rapid glycogenesis when fructose was substituted for glucose intravenously[166] and, when it was combined with amino acids, fructose added protein-sparing effects.[167] However, these were all short experiments. When the observations were extended over twelve to twenty-four hours or longer it became apparent that fructose conversion to glucose occurred, and the advantage of fructose over glucose became clinically less important.[168] The advantage, however, may still be enough during the first two hours of therapy to be useful in diabetic acidosis, in which insulin action on glycogenesis is markedly depressed. Several investigators used 5 per cent fructose solution in the first six hours of treatment of diabetic acidosis and believed that it was adequately utilized.[169-171] It should also be stressed that one of the best indexes of therapeutic progress, the blood sugar level, is not affected by the use of fructose as it is by glucose[165] in the first two to four hours of its administration.

Degenerative Complications

General. Certain physiologic attributes of patients with intercapillary glomerulosclerosis and retinopathy have been described as distinctive for them as compared with other diabetic persons. It had previously been observed that adrenocortical hyperactivity contributed to the development of these lesions experimentally both in diabetic and in nondiabetic subjects. Then histologic, physiologic[172] and biochemical evidence[173] was assembled for such hyperacidity in the diabetic patients with these complications, especially the renal. Since cortisone-treated animals retain injected vitamin B_{12} poorly, this phenomenon was investigated in turn and found also to be true of patients with diabetic retinopathy. Such patients excrete 40 per cent of a 50-microgm. test dose, twice the average for normal persons and five times that of ordinary diabetic patients.[174]

This may provide the first physiologic and biochemical basis for the clinical observation of the peculiar predisposition of certain persons to the development of pathologic complications of diabetes. Such persons stand out as exceptions in studies that are otherwise statistically valid in proving the quantitative relation between many diabetic complications and poor control.

It is generally apparent that degenerative changes in large (atherosclerosis) and small blood vessels, but not of the aorta,[175] are accelerated in diabetes. The metabolic mechanism is not clear, but there is at least a tendency for serum cholesterol and lipoproteins of the S_f 12 to 30 class to be elevated in diabetic patients,[176] particularly in female patients with hypertension and coronary atherosclerosis.[177] The correlation seems better with the lipoproteins than cholesterol in rabbit arteriosclerosis,[178] but in human patients the evidence is confusing.[176] A slow decrease in the elevated cholesterol of diabetic persons occurs with better regulation of the disease[179] or the substitution of vegetable for animal fat in the diet.[180] Yet a causal

relation to atherosclerosis has not been proved, so that at present the importance of the association is not much better understood than the observations regarding the disturbance in inositol[181] or polysaccharide[182] metabolism in diabetic patients with complications.

Atherosclerosis. Over the age of fifty the frequency of deaths from vascular disease of all types is 80 per cent greater among diabetic than among nondiabetic persons.[183] In life, this is manifested as a specific fortyfold increase of gangrene of the lower extremities among diabetic patients as compared with nondiabetic persons[184]; by comparison myocardial infarction is one and three-tenths times more frequent in males and fourteen times in females.[185]* There is thus a fourfold greater predilection for actual tissue necrosis in the legs as compared with the heart, even though post-mortem examination shows no such difference in the incidence of arteriosclerotic involvement of the vessels themselves in those two areas.[183]

Certain recent reports on peripheral circulation, especially the injection studies of Wessler and Schlesinger[186] and Wessler and Silberg,[187] have shed new light on this discrepancy. Narrowing of vessels alone, without occlusion, does not lead to gangrene. Quantitatively, the vessels of legs requiring amputation are occluded to over 25 per cent of their total length. Not only is the degree of vascular occlusion greater but also there is an even greater collateral circulation than that in infarcted hearts. The delicate equilibrium between the two processes is found in half the cases to have been upset by a new thrombus, which has extended by propagation to block important collateral channels.

Gangrene of the legs occurs with less vascular impairment among diabetic than among nondiabetic persons,[188] and even in the former the clinicopathological correlation is far from exact.[187,189] Attempts to explain this on the basis of dysfunction of small noninjectable vessels are not convincing.[190,191]† The discrepancies are due to a variety of unfavorable factors, both physiologic and pathologic, endogenous and exogenous. The internal include cardiovascular (shock, decompensation), humoral (anemia), neurologic (diabetic neuropathy), psychiatric (mental disease) and metabolic (diabetic acidosis, uremia) factors, many of which can be treated. The external factors include chemical, thermal or mechanical trauma, susceptibility to skin infection from poorly regulated diabetes and local predisposing defects of an anatomic (such as hammer toe) or pathologic (such as corns and calluses) nature. The last group, although preventable, precipitate the final series of events leading to amputation in 33 to 50 per cent of cases.[188,189] In a survey of 260 consecutive ambulatory diabetic patients in this clinic, 55 per cent were found to harbor such environmental handicaps.[192]

Although it is quite possible that good control can decelerate the atherosclerotic process in diabetes it is an even more optimistic note that, even in the face of this process, tissue necrosis can be indefinitely postponed by simple measures of foot care in the present diabetic population. In the Abraham Rudy Diabetes Clinic amputation attributable to such preventable synergistic factors has been reduced to a minimum by an intense program of patient education. In the event of sudden impairment of circulation, the evidence now points to the value of anticoagulants,[187,189] especially heparin.[193]

Renal Lesions

There is still disagreement regarding the pathology of intercapillary glomerulosclerosis. Most controversial has been the proposal to consider the diffuse form[194] of hyalinization of the glomerulus rather than the nodular variety alone as pathognomonic of the condition,[195,196] thereby increasing the frequency by 50 per cent. Some facts favor this point of view. Hypertension, the most common feature associated with the diffuse lesion in the nondiabetic person, is frequently absent in diabetes. The clinical syndrome is sometimes seen in patients with diffuse hyalinization alone.[194] Finally, the new Polaroid color-translating ultraviolet microscope reveals a distinctive orange color common to all diabetic glomeruli "independent of the degrees of the involvement in atrophy, sclerosis or intercapillary glomerulosclerosis."[197] Although the technic is still new, this finding tends to support the theory of a single cause of glomerular lesions in diabetes. The degree of arteriolar hyalinization in diabetic kidneys (as in the eye) is unique, even more severe than that of the nondiabetic patient with hypertension, and may occur in the absence of hypertension. This severe ischemic lesion is correlated with (though not pathognomonic of) severe intercapillary glomerulosclerosis and with obliteration of glomeruli, azotemia and renal failure.

Correlation of clinical and pathological findings is no better than in other types of renal disease.[198] It is better the severer the disease and is twice as good with the nodular as with the combined nodular and diffuse form.[199] Combining the clinical findings of moderate hypertension, albuminuria and edema increases the predictability of the pathologic lesion to 66 per cent. Bell[194] emphasizes the age difference in this respect. In youth the presence of hypertension is significant. In old age even moderate proteinuria or edema is commonly due to other conditions. To enhance diagnosis renal biopsy (nonoperative)[200] and fat stains of the urinary sediment[201] have been proposed as helpful.

The frequency of serious infection of the genitourinary tract is increased among diabetic patients. The type of organism frequently found and the pre-

*The specific increase in Sf12-30 lipoproteins in female diabetic patients with complications[176] was mentioned above.

†In these purely physiologic experiments, the large vessels were assumed to be normal by clinical methods alone. Wessler and Schlesinger[186] believe, from their injection studies, that clinical evaluation is not sensitive enough for this purpose.

dominance of infection in the female sex suggest a pathogenetic relation and possible prophylaxis by improved personal hygiene.[202] The permanent cure rate is now small (8 to 15 per cent) and depends on the eradication of the foci of infection or obstructive factors,[203] which can be discovered seven times as frequently if special genitourinary investigation is employed[203] as compared with ordinary means.[202] Moreover, the infection should be attacked by the use of modern bacterial-sensitivity studies and with antibacterial agents in sufficiently large doses and effective combinations. Finally, good diabetic regulation is important to ensure permanent eradication of infection.

The Eye in Diabetes

Retinal abnormalities in diabetes stem mainly from vascular alterations. However, it is still of interest that, unlike that of other tissues, the glucose utilization of retinal tissue in vitro is not influenced by hyperfunction or hypofunction of various endocrine organs, including the thyroid and pituitary glands, gonads and islands of Langerhans.[204]

Regarding the arterioles, Ashton[205] suggests that, as in the kidneys and elsewhere in diabetes, advanced arteriolosclerosis in a characteristic accompaniment of advanced retinitis. However, here, too, it is a separate entity. Pathologically, its end stage is occlusion, with obliteration of the distal arteriolar capillary bed without effective arterial new-vessel formation.

Ehlers,[206] from clinical observation, believes that, except for the earliest stages, proliferative diabetic retinopathy by its course is distinct from the nonproliferative form. As further evidence of this distinctiveness he cites its predilection for the young and the frequency with which a single type attacks both eyes of a given patient. In the therapy of retinitis, testosterone appears valueless in the ordinary variety,[207] but x-ray therapy has been reported as helpful in the more serious proliferating variety.[208]

In alloxan-diabetic rats, it has been noted that the cataracts that developed in seven to fourteen weeks regressed after two to four months of insulin therapy, even though treatment only partially improved the diabetes.[209] This occasionally occurs in the human form of the disease.

Neuropathy

Mirsky et al.[210] studied quantitatively the variation of vibratory perception in diabetic and normal persons at various ages. They found that vibratory sense, as measured by a quantitative vibrometer, diminished with age, but that diabetes accelerated the process by an average of twenty years.[210]

An unusual form of diabetic myelopathy has been redescribed recently. The symptoms consist of pain in the hips and thighs. It could conceivably be confused with other neurologic syndromes, since, as in other diabetic complications, the disease is frequently undiagnosed or of short duration. The diagnosis is important since improvement is contingent on the treatment of the diabetes.[211] The Charcot-like lesions of diabetes have been described in the vertebras, an unusual location.[212]

Vitamin B_{12} has been advocated as useful in the treatment of diabetic neuropathy. It is absorbed primarily in the duodenum[213] but so poorly, even in the normal person, that it is a hundred to two hundred times more effective by the parenteral route.[214,215] The recent availability of the more concentrated preparations (1000 microgm. per cubic centimeter) makes it possible to administer them mixed with insulin. By animal assay and human clinical trial I have found that vitamin B_{12} can be administered mixed with regular or modified insulin without decrease in therapeutic effectiveness of either medication.*

*Unpublished observations based on mouse assay for the action of regular insulin and human trial for modified insulin and vitamin B_{12}.

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MEDICAL INTELLIGENCE

ACCIDENTAL PASSAGE OF A POLYETHYLENE CATHETER FROM CUBITAL VEIN TO RIGHT ATRIUM*

Report of a Fatal Case

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REPORTS of foreign bodies in the myocardium or cardiac chambers are numerous, war missiles being the most common. Such objects have led to cerebral emboli from adjacent cardiac thrombi, subacute bacterial endocarditis and myocardial aneurysms.[1] Foreign bodies, especially needles, have passed along veins through the vena cava and into the right side of the heart, with resultant cardiac damage of varying degrees.[2] Cardiac catheterization can cause cardiac arrhythmias, mural thrombus formation and contusions of the myocardium.[3] Hemorrhage of the myocardium, thrombosis of the coronary sinus, pericarditis and myocardial fibrosis have also been reported.[4] McMichael and Mounsey[5] described 5 cases of adverse reaction to cardiac catheterization in which all the patients recovered. Syncope, probably caused by vasovagal reflex mechanism, may occur.[6]

In the case reported below, a polyethylene catheter passed from the right median cubital vein to the right atrium. To the best of our knowledge this is the first such case recorded.

CASE REPORT

A 54-year-old housewife weighing 250 pounds was admitted to the hospital on April 7, 1954, complaining of severe, compressing precordial pain of a few hours' duration. Electrocardiographic study confirmed a diagnosis of myocardial infarction. She had had long-standing hypertension treated by sympathectomy 8 years before. An epidermoid carcinoma, Grade 2, of the bladder 1 year previously had required total cystectomy, with bilateral ureterosigmoidostomies and panhysterectomy.

The blood nonprotein nitrogen was 100 mg. per 100 cc. The patient was dehydrated and unable to retain fluids given by mouth. During vigorous attempts to restore normal hydration parenterally, most of the accessible veins became thrombosed. On the 33rd hospital day, through a 3.5-cm. transverse incision in the right antecubital space a No. PE-60 (Clay-Adams Co. ID. 030 OD .048) polyethylene catheter, 22 cm. in length, was inserted into the right median cubital vein and fitted with a No. 18 trochar needle. The vein was ligated distally after transection, and the catheter was tied into the vein proximally with silk. Both the catheter and the needle were separately secured to the skin with adhesive tape. The skin margins were approximated with 3 interrupted silk sutures. After 2 days of constant use for glucose in water, and saline infusions, the polyethylene tubing disappeared, during an especially fitful bout of restlessness. Palpation of the extremity did not show the catheter to be in the vein or the surrounding soft tissues. A 2d incision for the purpose of infusing solutions was later performed in the right lower extremity. The patient died two days later.

Autopsy demonstrated a recent occlusion of the right coronary artery with a large posterior and apical myocardial infarct. There was evidence of old infarction as well, and 4 cm. of the polyethylene catheter was found in the right atrium, extending up the superior vena cava for a distance of 18 cm. The end of the catheter rested against the tricuspid-valve ring. At the level of the end of the catheter, on the anterior wall of the right atrium, was a mural thrombus measuring 2 cm. in diameter, presumably the result of atrial contraction against the blunt end of the catheter. Microscopical examination disclosed myocardial necrosis beneath the mural thrombus in this region. The catheter was surrounded by a thin layer of ante-mortem blood clot, and the entire right side of the heart was filled with similar material (Fig. 1). There was residual epidermoid carcinoma in the pelvic soft tissues, with thrombosis of the right iliac vein. Death was ascribed to myocardial infarction.

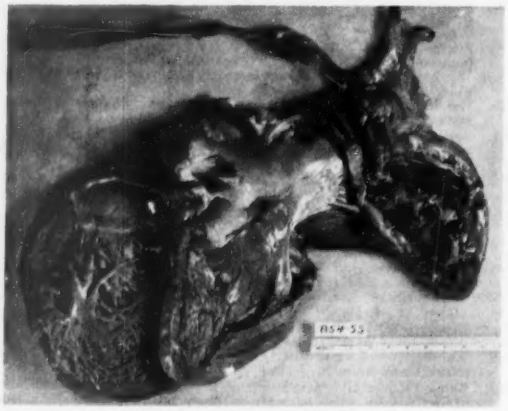

FIGURE 1. *Opened Heart with the Right Ventricle on the Right Side.*

The catheter is shown in the right atrium resting against the tricuspid-valve ring. At the top of the illustration the ante-mortem thrombus around the portion of the catheter that lay in the superior vena cava is demonstrated.

DISCUSSION

The widespread use of intravenous catheters for infusion makes it desirable to recognize the potential seriousness of complications if effective methods for securing the apparatus in place are not employed. The most usual and satisfactory method is to tie the catheter to the vein and also to suture the skin with interrupted silk, leaving one thread long with which a length or loop of catheter is tied. A further length of catheter can be taped to the arm or an arm board as a further safeguard.

SUMMARY

What is believed to be the first case in which a polyethylene catheter inserted into a vein for the ad-

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ministration of fluids escaped and lodged in the right atrium is reported. Suggestions for avoiding such a complication are made.

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BY THE LONDON POST

Science and Human Nature — The Cost of Drugs

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OXFORD has always been closely linked with the British Association for the Advancement of Science. Its first annual meeting was held there in 1832 and since then it has revisited Oxford four times. It was at a meeting in 1880, just after the publication of Darwin's *Origin of Species*, that Bishop Wilberforce asked Dr. T. H. Huxley whether it was through his grandfather or his grandmother that he derived his ancestry from the venerable ape.

Dr. E. D. Adrian, O.M., P.R.S., recalled this famous incident in his presidential address to the Association, which met in Oxford again this year. He pointed out that within a few years of the 1880 meeting the battle for Darwin's theory was won and it seemed that the discoveries of science had forced men to give up beliefs on which they had relied for centuries. Today, he said, his own generation faced discoveries that might spell the end of all human aims. Referring to the atomic bomb, he said that one could regret that atomic bombs are possible without regretting the discoveries that led to them. Indeed, he thought that man's fate was in his own hands, and he suggested that if human behavior could be made worthy of increased knowledge, one could live safely. He thought that the next great scientific advance should come from the study of social science. To this end the scientist must apply his science to learn as much as possible about the mental and physical cause of human behavior, and he must study human nature to prevent its failures. Although there was some distrust of the methods used in social science, Dr. Adrian considered it a most important scientific development. He believed that the scientific investigation of mankind would help the process of civilization, and he made a plea for more social scientists in universities. He also stressed the value of a university education: the critical outlook that a university training encouraged was a vital factor in helping men to use their knowledge for solving the new problems of the times.

In his concluding remarks he urged the Association to encourage every kind of scientific inquiry, remembering that "it is human nature to inquire, to learn by experiment and to profit by what it finds out."

The subsequent meetings of the fourteen sections of the association ranged over a wide field. Physicists and chemists, botanists and zoologists, physiologists and psychiatrists all had their say. Nuclear physics was naturally a prominent subject, and Sir John Cockcroft, president of the section of physics, discussed the game of "voltage billiards." He likened the protons, mesons and whole atomic nuclei to balls with several million-volt cyclotrons as cues to impel them.

Passing from the sublime to the ridiculous, the child psychologists were somewhat startled to learn that since nearly 50 per cent of normal children indulge in thumb sucking, there is not much to worry about. A child psychiatrist maintained that, to the child, thumb sucking is merely a pleasant and harmless way of passing the time until the next meal and that as a habit it deserves the same consideration as that achieved by smokers at a later age. He suggested that a well sucked thumb is much less toxic than a well smoked pipe.

It is perhaps no wonder that the first Association meeting a hundred and twenty-two years ago was scurrilously described as a "hodge-podge of philosophers" — the same charge might be made today. Nevertheless, as the *Lancet* has pointed out, the Association has always aimed at familiarizing the lay public with the scientific attitude and the fruits of scientific thought, and for this reason, the program cannot avoid being somewhat unwieldy.

* * *

The size of the national drug bill continues to exercise the minds of economists and politicians. At the outset of the National Health Service the expenditure on prescriptions rose, and the Ministry of Health thought that the pharmaceutical manufacturers did well out of the health service because it increased their business. In particular it was considered that there was excessive prescribing of high-priced proprietary preparations. For this reason an investigating committee was set up under the chairmanship of Sir Henry Cohen. This committee noted the three distinct classes of product that the industry recognizes: basic or standard drugs as listed in the *British Pharmacopoeia;* ethical proprietaries, which are drugs made under trade names but advertised solely through medical mediums; and drugs advertised to the public. The committee recommended that preparations advertised to the public should not be prescribed under the National Health Service. It then examined the composition of 6000 ethical proprietaries with the object of deciding whether they were therapeutically worth

their cost. As a result it recommended that proprietary preparations for which there is a standard pharmacopoeial equivalent should only be prescribed if satisfactory price arrangements could be made between the Ministry and the manufacturers. The industry has been critical of these recommendations, contending that proprietaries are not inevitably more expensive than the standard equivalent. Although this contention is often true, there are a few cases in which the difference between the cost of the proprietary and the standard equivalent is so wide that it is difficult to justify.

Nevertheless, the industry resents the application of rigid and unimaginative principles of accountancy to pharmaceutical costs. The manufacturers of successful proprietaries have to cover their own research costs and also the cost of unsuccessful projects. The industry also resents the principle of a standard rate of profit, on which it fears the Ministry may base its price policy. The *Times* points out that it has been suggested that the National Health Service provides a steady market and so takes the risk out of the business. This is not true because, although the demand for staple drugs may not vary, the demand for new drugs is uncertain. Dr. Fleck, the chairman of Imperial Chemical Industries, has recently asserted that it is not enough for the annual expenditure on research to be covered as a cost. The risks inherent in research and the marketing of new products must be reflected in profits. He suggested that there is a danger that pharmaceutical research might be rendered so unattractive that this important field might be abandoned by one company after another. As the *Times* points out, it would be ironical if the introduction of the National Health Service was allowed to have this effect.

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 40431

PRESENTATION OF CASE

First admission. A sixty-nine-year-old retired businessman was admitted to the hospital because of mild prostatism of four years' duration.

Four episodes of sudden, severe weakness lasting from a few minutes to as long as half an hour occurred during the two years before admission. There had never been any accompanying chest pain, discomfort, unusual dyspnea or dependent edema. At least one such attack occurred after a meal.

Physical examination revealed only a soft, nontender prostate gland of about twice the normal size. The heart, lungs and abdomen were normal.

The temperature, pulse and respirations were normal. The blood pressure was 230 systolic, 125 diastolic.

Routine studies of the urine and blood were negative. Roentgenograms of the chest revealed some enlargement of the left ventricle and a tortuous aorta. Intravenous pyelograms were normal.

On the third hospital day a transurethral resection was performed. The pathological report was benign prostatic hypertrophy. The postoperative course was uneventful until twenty-four hours after operation, when the patient experienced an episode of weakness, sudden in onset and associated with "fogging of vision." Shortly thereafter he complained of severe pain in the left side of the chest anteriorly, with radiation into the neck. He broke out in a cold sweat and became very pale. When seen by a physician half an hour after onset he exhibited slight cyanosis, and the radial pulsations were absent. The systolic blood pressure was 40, and the heart rhythm was regular at a rate of 48. The chest pain was no longer present although he did complain of "gas pains" in the upper abdomen. In the next half hour, the pulse gradually rose to 72, and he began to feel entirely well. The blood pressure had risen to 90 systolic, 60 diastolic. An electrocardiogram taken during this period of gradual improvement revealed a normal rhythm at a rate of 55 and no abnormalities except low and slightly notched upright T waves in Leads CF_4 and CF_5. Twelve hours after the onset he was asymptomatic, with a blood pressure of 145 systolic, 80 diastolic, and a regular pulse at a rate of 72 a minute. Another electrocardiogram on the second postoperative day disclosed no significant change. The rate was a trifle faster, and the T waves were slightly higher. On the third postoperative day he had a transitory episode of weakness, again sudden in onset and occurring while he was in bed, which was associated with flushing and lasted only a minute or two. On examination five minutes later the pulse was 60 and regular. After this episode he was given ephedrine along with mild sedation. Therefore, he remained symptom free and was discharged on the eighth hospital day.

Final admission (five and a half years later). In the interval he had remained well, without recurrent syncopal attacks or any other symptoms referable to the cardiorespiratory system. Four hours before entry, while preparing lunch, he suddenly experienced a severe sharp pain in the throat that then radiated to

the jaw bilaterally and down to the midsternal region. The pain also extended down both arms to the elbows and was associated with mild nausea, coldness of the hands and some sweating; after its initial appearance it was described as continuous, dull and aching. After about two hours he was seen by his physician, who administered Demerol.

On admission two hours later the patient was in no acute distress and was alert and well oriented. Ophthalmoscopic examination revealed bilateral early cataracts; the fundi were not well visualized. The neck veins were not distended, and the lungs were clear. The left border of the heart was at the upper limits of normal to percussion. The apical rate was 68 without pulse deficit. Occasional premature beats were noted. The heart sounds were of good quality, and there were no murmurs. The aortic second sound was greater than the pulmonic. The abdomen was normal, and the remainder of the examination was negative.

The temperature was 97°F., the pulse 68, and the respirations 18. The blood pressure was 165 systolic, 100 diastolic.

Urinalysis was negative. Examination of the blood showed a hemoglobin of 14.4 gm. per 100 cc. and a white-cell count of 11,300, with 88 per cent neutrophils. The serum nonprotein nitrogen was 23 mg., and the fasting blood sugar 101 mg. per 100 cc. An electrocardiogram disclosed the appearance of a QS complex in Lead aVF and flattening to inversion of the T waves since the previous tracing.

The patient was put on bed rest and sedation. On the second day he was comfortable although complaining of some residual arm pain and mild headache. The physical findings were unchanged except for a temperature of 101°F. He was given quinidine and anticoagulant therapy. On the next day the headache persisted, and in addition there was some precordial pain, which was related to respiration. No pleural or pericardial rub was audible, and the lungs were clear. The cardiac rhythm had become irregular; electrocardiograms revealed a wandering pacemaker. Little other change was noted except for slight elevation of the ST segment in Lead aVF. The sedimentation rate was 6 mm. in one hour, and a second white-cell count was essentially unchanged. The dosage of quinidine was increased. On the fourth hospital day he continued to complain of chest pain, which now had migrated to the right of the sternum. It still was distinctly related to respiration. Again, no rubs were heard, but for the first time crepitant rales were noted over the right base. The cardiac rhythm remained irregular. An x-ray film of the chest taken with the patient supine showed little change from the film of the previous admission except for a slight increase in tortuosity of the aorta. Later the same day slight right-calf tenderness was elicited, but comparative measurements were equal and no edema was present. During the following day his condition remained unchanged. The temperature had gradually fallen to 99°F. The sedimentation rate was 48 mm. in one hour; the white-cell count was 11,600, with 81 per cent neutrophils. An electrocardiogram demonstrated a sinus arrhythmia with a rate varying between 65 and 85 a minute. Changes since the previous record were in the direction of normal.

On the sixth hospital day a severe chest pain to the left of the sternum suddenly developed, with radiation down the right arm and up into the neck and jaw. At the same time the patient noted increased severity of headache and some nausea. The pulse was 78 and regular; the respiratory rate was 24, and the blood pressure 180 systolic, 100 diastolic, and 190 systolic, 100 diastolic, for the left and right arms respectively. There were no murmurs or rubs. A few crepitant rales were present over both lung bases. Examination of the legs was negative. With Demerol the pain gradually subsided in about thirty minutes to an hour. Administration of Randixin, 50 mg. thrice daily, was started and Dicumarol was discontinued. Up to this time the prothrombin time had ranged between 43 and 64 per cent of normal.

During the next three days, the patient complained only of mild headache. The pulse remained regular, and the blood pressure was stable at 160 systolic, 100 diastolic. A few rales persisted over both bases. Another electrocardiogram on the seventh hospital day revealed no significant change since the last tracing. The prothrombin time by the eighth hospital day was 75 per cent. On the tenth day he suddenly became pale and began to perspire profusely. The blood pressure was unobtainable. The neck veins were neither distended nor pulsating. The heart sounds were barely audible. There was no dyspnea. An electrocardiogram demonstrated a sinus tachycardia at a rate of 120; the PR interval was 0.12 second. The T waves were upright in Leads 1, 2, V_2, V_3, V_4, V_5 and V_6 and inverted in Leads 3 and V_1. The ST segments were slightly elevated in Lead 2 and greatly elevated in Leads V_1 through V_5. He was given vasopressors by constant drip but remained in shock for about four hours, during which he complained of severe precordial pain. The blood pressure gradually rose, and the chest pain subsided. He was digitalized. Sixteen hours after the onset of the hypotensive episode the blood pressure had climbed to 140 systolic, 110 diastolic, and the pulse rate had fallen to 94. He again began to have mild pain in the anterior portion of the chest that persisted. The blood pressure remained stable. On the next day the white-cell count was 19,300, with 97 per cent neutrophils. Later during the same day, twenty hours after the onset of shock, he suddenly died.

Differential Diagnosis

Dr. Robert S. Palmer*: The question I have to consider is not what disease but which cardiovascular disease was present.

*Physician, Massachusetts General Hospital.

The episodes of weakness in this elderly man, who, we may assume, had the normal aging processes in the blood vessels, may have been due to the carotid-sinus syndrome. A carefully taken history might have revealed a tendency to fainting throughout his life—a congenital susceptibility to vasovagal syncope. He may have had transient heart block with Stokes–Adams seizures or, indeed, any of the causes of cerebral anemia. The history, in short, does not differentiate benign and serious fainting. The physical examination revealed hypertension, which we expect in 50 to 60 per cent of men at his age. Moreover, patients over sixty commonly show some prominence in the region of the left ventricle with or without hypertension. The tortuosity of the aorta may be normal in this decade of life. What annoyed the patient was not his vascular sclerosis but his dwindling urinary stream. This his advisers elected to relieve, a thing not to be done lightly or inadvisably as we shall see.

Three days after operation he experienced a pain in the left anterior part of the chest and neck, with hypotension and a slow pulse, the electrocardiogram showing only nonspecific T-wave changes, which promptly returned to normal. From his treatment and early discharge, his doctors apparently concluded that he had simple benign fainting (the slow pulse), not myocardial infarction. They may properly have thought of heart block though this was not demonstrated by the electrocardiogram. Doubtless, they considered the carotid-sinus syndrome. He also had "gas pains" in the abdomen. Possibly, aortic dissection crossed their minds as it does mine and, to complete the preliminary differential diagnosis, pulmonary infarction must be mentioned. Of these possibilities we have no evidence for the last. Nothing seriously suggests aortic dissection. Statistically, myocardial infarction is most likely. Fainting is not especially characteristic, but this man was subject to fainting and, indeed, hypotension from whatever cause may induce myocardial infarction in a person with asymptomatic coronary-artery disease. Early electrocardiograms with incomplete precordial exploration may miss a small infarct. If he had heart block or a sensitive carotid sinus we do not know about it, nor may we expect the autopsy to confirm or deny our suspicions.

At this point I agree with his advisers that he had benign fainting, with or without a sensitive carotid sinus or the more remote possibility of transient heart block. Indeed I must agree, since he was well for five and a half years without symptoms referable to the heart and no fainting. This weighs heavily against heart block and the carotid-sinus syndrome. There remains, in spite of a symptom-free period of five and a half years, the statistical possibility of a small myocardial infarct.

Four hours before the final admission a new condition, which led to his death eleven days later, was added—sudden severe pain in the throat, midsternum, jaws and arms, which persisted without initial vascular shock and without signs of congestive heart failure. There were no early acute T-wave or ST-segment changes characteristic of myocardial infarction, and the T-wave pattern improved as early as the fifth day. The sedimentation rate was normal, and the white-cell count minimally elevated. The sudden onset without premonitory symptoms, the severity of the pain, the absence of initial shock, the appearance on the second day of headache and its persistence make aortic dissection the foremost possibility in my mind. The pain and its distribution, but not the headache, could have been due to myocardial infarction or coronary insufficiency. Furthermore, the latter may be caused by aortic dissection and encroachment on the mouths of the coronary arteries. The relation of the chest pain, which had extended to the right, to respiration and the finding of rales and tenderness of the right calf remind me to include thrombophlebitis and pulmonary infarction as the third possibility. Calf tenderness I find a very unsatisfactory sign since so many patients without thrombophlebitis have it. Those in charge of the patient were thinking of this or of myocardial infarction, for they prescribed Dicumarol.

Sinus arrhythmia, which is somewhat unusual for a man of this age, is sometimes said to be related to coronary-artery disease. The electrocardiographic changes on the fifth day were in the direction of normal, and strongly against myocardial infarction in spite of persistent pain. When a patient has angina one may expect some change in the tracing. Up to this time it had shown nothing specific. Nevertheless, in my opinion, the pain was consistent with myocardial infarction, having been present mainly in the middle third of the anterior portion of the chest, with radiation to the jaw and the arms.

The headache from the second day on is most unusual and is not explained by myocardial infarction. In the acute stages of myocardial infarction the psyche has room only for symptoms of that condition, which threatens life, not for aches and pains from incidental affairs; therefore, this headache of increasing severity I take to have been a part of the condition that killed the patient, and I think it proved to be aortic dissection. The difference noted in blood pressure in the two arms is not significant, but the fact that it was observed and recorded is. I like to think of the motions the physicians' agile minds were going through. First they thought of myocardial infarction and said, "Quick, boys, let's get his prothrombin time down." Then they thought of aortic dissection and said, "Heavens, let's get his blood pressure down and stop the anticoagulants so that when he ruptures into the pericardium he won't bleed so fast."

Did he have a myocardial infarction? I cannot positively make a diagnosis of myocardial infarction on the electrocardiogram or clinical data at either the first or the final admission though I consider it a reasonable statistical possibility at the first and a likely secondary result of aortic dissection, which I think

was the primary cause of his death. The severe and persistent headache in the final illness is not explained by myocardial infarction, and typical electrocardiographic changes of a progressive development would ordinarily have been seen in the course of a week. Furthermore, there was not the persistent hypotension of medical shock that we expect in severe fatal myocardial infarction. Of course, aortic dissection may cause coronary ischemia or even closure, explaining the precordial ST-segment elevations found twenty-four hours before death. Did he have pulmonary infarction deriving from leg or pelvic thrombophlebitis? There is nothing in the history, physical examination or x-ray study from which I can positively say he did or did not have pulmonary infarction, but I see no reason to suppose that if it was present it was other than incidental since what I suppose he died of fully explains all that happened.

Did he have aortic dissection? The fact that he had an equivocal or indefinite electrocardiogram, a sharp fall and a prompt rise of blood pressure, with diffuse pain, is suggestive. One would like to hear about a sudden, tearing, extremely severe pain, the dissection rending the aorta and proceeding downward until the legs became pulseless. We do not often have so perfect a picture. Nevertheless, the intensity and extent of the pain, including the headache, the fall, followed by, at first, rapid recovery of the blood pressure and the absence of a typical unfolding electrocardiographic picture of myocardial infarction make aortic dissection the most likely diagnosis. The sudden shock with near disappearance of heart sounds indicates rupture, probably into the pericardium.

Could the original dissection have occurred five years previously? In short had he had a double-barreled aorta for over five years? I have seen 1 such patient autopsied in this hospital. In the present case, if the dissection had occurred five years previously, it might have caused the cerebral symptoms by dissection of the neck vessels. Certainly, in the final illness, such an extension along the great vessels may explain the headache.

Dr. John B. Graham: I saw this man in the last three years of his life. He had had choking spells at night after he had gone to sleep; they were interpreted as being due to food regurgitated into the esophagus.

Dr. Palmer: Not just in the last five years? A large aorta sometimes produces choking.

Dr. Graham: He had had the episodes for at least twenty-five years.

About thirty hours before the last admission, he complained of chest pain. Early in the morning he had been awakened by the most severe choking spell he had ever had. An upper gastrointestinal series for that complaint showed no diaphragmatic hernia or esophageal difficulty. Between the two hospital admissions he had an episode that might have been related to the cardiovascular system. After he had wrestled with a police dog, trying to make it behave, he had pressure in the chest and dyspnea lasting half an hour. At that time two electrocardiograms, one taken shortly afterward and one ten days later, showed flat T waves throughout. I think it is correct to emphasize that headache was a very prominent symptom in the last illness. We found on closer questioning that the headache started immediately with the first pain and continued as the most prominent symptom throughout the hospital stay.

Dr. Palmer: Did he have a carotid-sinus syndrome?

Dr. Graham: I do not know; I was not acquainted with the history of fainting spells, and I did not test that. I certainly did not go out of my way to test it in the last illness. I did believe that the carotid pulses were slightly more tender than usual, but both had pulsations in them.

I must say that Dr. Palmer is a good mind reader.

Clinical Diagnoses

Coronary-artery disease.
Acute myocardial infarction.
Generalized arteriosclerosis.

Dr. Robert S. Palmer's Diagnosis

Dissection of aorta, with rupture.

Anatomical Diagnoses

Dissecting aneurysm of ascending aorta, with rupture into pericardial sac and cardiac tamponade.
Myocardial infarcts, recent and old, small.
Coronary sclerosis.

Pathological Discussion

Dr. Winfield S. Morgan: Dr. Palmer's diagnosis was absolutely correct.

At autopsy, except for the liver, which weighed 1650 gm. and showed severe central congestion, the pathologic changes were confined to the chest. The lungs were moderately increased in weight and showed congestion and edema, and there was about 25 cc. of clear fluid in each pleural cavity.

The pericardial sac was greatly distended and contained 650 cc. of fluid and clotted blood. The cause of this was a dissecting aneurysm of the aorta: 6.5 cm. above the aortic valve there was a complete transverse tear in the aortic wall, leading into a large blood-filled space. Distally, the dissection extended as far as the level of the left subclavian artery and surrounded the orifices of the other great vessels. There was no dissection into the walls of these vessels and no apparent encroachment on their lumens although one cannot be certain of their state during life, and the dissection near the orifices of the great vessels may explain the headaches. Proximally, the dissection extended to the ostium of the right and very close to that of the left coronary artery. Anteriorly, about 1 cm.

above the aortic valve, there was a 1.3-cm. rent in the adventitia communicating with the pericardial sac.

Microscopical study showed early but definite organization about the hematoma consistent with eleven days' duration, and we believe that the initial episode that brought the patient to the hospital on the final admission represented the time when the dissection occurred. The sections of the aorta showed the muscle-degeneration type of change in the media rather than loss of elastic fibers. This is in accord with the findings of Gore and Seiwert,* who observed that the degeneration of elastic fibers was more often seen in a younger and the muscle degeneration in a somewhat older age group.

The heart weighed 370 gm. and showed only moderate hypertrophy of the left ventricle. The right coronary artery was severely atherosclerotic, the lumen being narrowed to 0.1 cm. in places, and in the posterior aspect of the left ventricle and interventricular septum there was an old, densely fibrous scar consistent with the occurrence of a small infarct during the first hospitalization five years before death. In the apex of the left ventricle there was a fresh infarct of several days' duration. There were no thrombi in either coronary artery, and this recent infarct may have been due to encroachment on the lumen by the dissection.

CASE 40432

Presentation of Case

An eighteen-year-old blind girl was admitted to the hospital because of a painful swelling of the left knee.

She first became aware of an occasional fleeting discomfort in the knee six months before entry. The pain was at first transient, became a constant dull ache, was intensified by motion and strenuous exercise and caused her to limp slightly. It was occasionally present at night. At the time of the initial appearance of symptoms she was put on bed rest and aspirin for a week. The pain was relieved only slightly, but she resumed her usual activities, protecting the knee from undue strain and thus got along satisfactorily. In the ensuing months the pain gradually lessened, and the limp became less noticeable. A week before admission she twisted the left leg while going downstairs; immediately, pain and swelling of the posterolateral aspect of the left knee developed, and once more the limp appeared.

She had been blind since infancy as a result of congenital cataracts and glaucoma. Her general health was otherwise satisfactory.

Physical examination revealed a pale girl, of small stature. The stance and posture were normal. There was a marked antalgic limp on the left side. Knee motions were almost equal, both actively and passively; the left knee lacked 5 to 10° of full extension, and pain limited flexion beyond 140°. The circumference of the left knee at the midpatella was 36 and that of the right 33 cm.; the measurements of the midthigh were 47 cm. on the right and 41 cm. on the left, and those of the calf 34 cm. on the right and 32 cm. on the left. There was a visible and palpable swelling in the left popliteal space over the lateral femoral condyle. The mass was soft, compressible and tender and did not transilluminate. The remainder of the physical examination was within normal limits.

The temperature was 98.6°F., the pulse 70, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

Urinalysis was negative, as was a test for Bence-Jones protein. Examination of the blood showed a hemoglobin of 13.0 gm., a white-cell count of 6200 and an erythrocyte sedimentation rate of 10 mm. in one hour. The blood calcium was 10.6 mg., the phosphorus 3.6 mg., the alkaline phosphatase 2.6 units, and the total protein 8.1 gm. per 100 cc. Roentgenograms of the knees revealed an expanding area of bone destruction in the lateral condyle of the left femur, the inner margin of which was obscure. The area of destruction was not loculated. The inferior portion of the lateral cortex of the condyle was elevated, and the superior portion was destroyed (Fig. 1). Lateral to the area of bone destruction was a small soft-tissue mass; no ray formation was noted. The joint surface was not involved. A roentgeno-

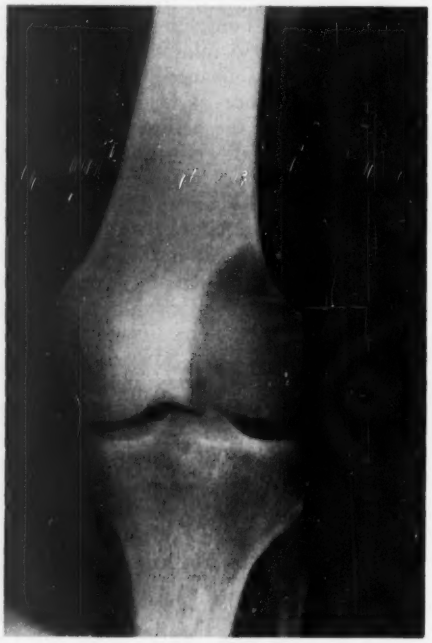

FIGURE 1. *Anteroposterior View of the Left Distal Femur, Showing the Large Area of Destruction Involving the Lateral Femoral Condyle.*

*Gore, I., and Seiwert, V. J. Dissecting aneurysm of aorta: pathologic aspects: analysis of eighty-five fatal cases. *Arch. Path.* **53**:121-141, 1952.

gram of the chest was normal. The skeletal survey showed no other bony lesions.

On the seventh hospital day an operation was performed.

Differential Diagnosis

Dr. J. Reginald Lingley*: The radiologist's description of the lesion in the protocol is very accurate. The lesion is entirely osteolytic (Fig. 1). It lies chiefly in the distal epiphysis of the femur but extends over onto the metaphyseal side. Its medial border is sharply defined and noninfiltrating, whereas the lateral border is irregular. A pathologic fracture has occurred in the lower part of the lateral cortex. The upper part of the lateral cortex looks irregular, apparently owing to active bone destruction. The faint outline of a small soft-tissue mass is visible chiefly in the lateral view posteriorly. It will be noted that there is no edema of the overlying soft tissues and that, in spite of the fact that the lesion extends right up to the articular cortex, there is no break in that cortex. There is no evidence of cartilage destruction and no fluid in the joint.

In the differential diagnosis I think that we must consider first infection, particularly tuberculosis, which is the most common infection that may be purely osteolytic. Other, much less common, purely bone-destructive lesions include typhoid and mycotic infections. However, I am willing to rule out all infections in this case. I believe that an infection that produced this large amount of bone destruction so close to a joint would have caused more evidence of joint involvement, as shown by fluid in the joint, soft-tissue edema, destruction of articular cortex and possibly some narrowing of the cartilage spaces. Furthermore, the clinical findings of normal temperature, white-cell count and sedimentation rate are against infection.

Other conditions that I should like to mention, only to eliminate, are the general metabolic disorders, endocrine disturbances and more or less generalized diseases of bone of unknown etiology. In this case the survey of the skeleton showed that the mass in the femur was a solitary lesion so far as we can discover by radiographic means. Furthermore, the other bones were all of normal structure and mineralization, and the blood chemical findings were normal. Hyperparathyroidism, polyostotic fibrous dysplasia and the many other conditions that affect several bones can be safely eliminated.

This brings me to tumor or granuloma, and perhaps that is where I should stop. So many types of tumor, both benign and malignant, may simulate one another and also the granulomas that sometimes the radiologist is wise if he simply says tumor and advises a biopsy. However, it is always a stimulating accomplishment for the radiologist to make a histologic diagnosis ahead of the pathologist, and we like to try, realizing our limitations. If this was a tumor it was probably a primary one since no other lesions were discovered on skeletal survey, the chest was normal, and there was no known primary lesion elsewhere in the body. Was this primary tumor or granuloma benign or malignant? The sharp, noninfiltrating medial border is in favor of a benign lesion, but the irregular lateral border suggests active bone destruction by a malignant process. I shall consider the primary malignant tumors to see how they fit this case.

Osteogenic sarcoma is the most common — it occurs frequently at this age and it may be entirely osteolytic, as this lesion was. However, the site of predilection of osteogenic sarcoma is in the metaphysis, and by the time it involves the epiphysis there is usually ray formation and periosteal lipping. I think osteogenic sarcoma is unlikely.

Ewing's sarcoma usually involves the diaphysis or metaphysis, and although in its early stages it may be entirely osteolytic, by the time the destruction has reached this stage there should be some onion-peel periostitis or ray formation.

Plasmacytoma is unlikely because of the age and sex of the patient. Myeloma occurs most often between the ages of fifty and seventy years and is somewhat more common in males. Myeloma has occasionally been observed in young males, but I think it would be unlikely in eighteen-year-old females.

Reticulum-cell sarcoma also occurs in the older age groups, but it usually shows more osteoplastic activity.

Of the primary benign tumors and granulomas nonosteogenic fibroma, fibrous dysplasia and benign bone cyst almost always occur in the diaphysis or metaphysis, and I shall not consider them as likely possibilities.

Osteoid-osteoma, unless it occurs in a phalanx, produces more sclerosis of bone about the central nidus, and the nidus is usually small.

Chondroblastoma occurs between the ages of twelve and twenty-five years and has a predilection for the proximal epiphysis of the humerus, but may occur in the epiphyses about the knee. However, it is usually found before the epiphysis has closed and usually has more granular calcification within it. It is four times as common in males as in females. I shall rule it out on the last three counts.

Eosinophilic granuloma is a good possibility. When I first looked at this film I thought first of eosinophilic granuloma. It occurs frequently at this age but usually arises in the metaphysis or diaphysis rather than in the ends of the bones. I think it is a possibility, but I shall not pick it as the first diagnosis because of the location.

Enchondromas occur most frequently in the phalanges but may appear in any bone near cartilage. Out of 22 cases reported by Coley,[1] 4 affected the femur. When they are present in an epiphysis they may exactly simulate giant-cell tumors. I cannot rule out chondroma or even chondrosarcoma in this case.

*Radiologist, Memorial Hospital, Worcester.

The most common lesion in this group is the giant-cell tumor, which is usually benign but may, of course, be malignant. In addition to being the most common these tumors occur most often in the cancellous ends of long bones, particularly the lower femur, the upper tibia, the lower radius and the upper fibula. The highest prevalence is between the ages of twenty-one and thirty-five years, but they may occur between ten and twenty. They affect the two sexes equally. Viewed radiographically they are expansile and cystic appearing, with irregular trabeculation. They occasionally erode the cortex and sometimes break through it to form a soft-tissue mass.

In spite of the fact that this lesion was not trabeculated and showed little expansion I believe that statistically giant-cell tumor is first in probability among the tumors that I have mentioned. I shall make giant-cell tumor, benign or malignant, my first diagnosis and should certainly advise a biopsy.

Clinical Diagnosis

Giant-cell tumor of femur.

Dr. J. Reginald Lingley's Diagnosis

Giant-cell tumor of femur.

Anatomical Diagnosis

Giant-cell tumor of femur.

Pathological Discussion

Dr. David Kahn: Dr. De Lorme, will you tell us the preoperative diagnosis and your findings at operation?

Dr. Thomas L. De Lorme: The lesion was approached through a direct lateral incision. There was no evidence of extension of the lesion into the subcutaneous soft tissue or skin. The fascia lata was divided, and a tumor was encountered. The lesion itself did not seem to invade the soft tissues. There was very little cortical bone remaining over the tumor site. The tumor tissue was dark reddish purple, friable and moderately vascular and appeared to be poorly encapsulated. It took up the greater part of the lateral femoral condyle. The majority of the tumor was removed as one large globular mass, and the wall was curetted. The knee joint was entered in the procedure, and as much as could be visualized appeared to be normal. The defect was then filled with barrel staves of bone-bank rib. We believed that this was not a malignant giant-cell tumor and that the insertion of the graft would aid healing of the cavity. If it was a malignant giant-cell tumor the insertion of the graft would do no harm since amputation would follow anyway.

The patient was immobilized for three weeks after the operation and had a benign postoperative course. The wound healed rapidly, and the sutures were removed in ten or twelve days.

Dr. Kahn: We received 19 gm. of curetted material in the laboratory. The histologic picture was similar in all parts examined and, as Dr. Lingley predicted, was that of a giant-cell tumor of bone composed of two types of cells: stromal cells, which were spindle or ovoid in shape, and large giant cells, which contained 30 or more nuclei and which are thought to result from fusion of the stromal cells. There was only a mild degree of atypicality of the stromal cells, and only a few mitotic figures were found.

Jaffe and his associates[2,3] have aptly named the giant-cell tumor "the problem child" among the benign tumors of bone. This is because with present knowledge it is almost impossible to predict the biologic activity or the prognosis of an individual tumor. From the experiences of Jaffe, Lichtenstein and Portis[3] and Lichtenstein,[4] and from a recent review of 101 cases at the Mayo Clinic,[5] certain generalizations have been possible. The first is that a very small percentage, 2 out of the 101 cases of the Mayo Clinic group, will have the criteria of malignancy at the first operation. If the lesion is treated by total excision, when that is possible, or if amputation is done as a primary procedure, no further trouble need be anticipated. If the lesion is properly treated about 50 per cent of patients will have no further trouble, about 40 per cent will have a recurrence or recurrences, and in 10 per cent malignant changes will finally develop. At present the consensus seems to be that we have no way on histologic grounds to predict with any degree of accuracy which of these tumors might recur and which might eventually become malignant.

Dr. J. T. Heyl: Do you ever see metastases, without local recurrence?

Dr. Kahn: It has been said that "an occasional giant-cell tumor may run a malignant course without presenting, even in its metastases, an obviously malignant histological pattern."[2] We have had no cases of that sort here. Malignant change may be evident at the first recurrence, or it may not develop until after repeated local recurrences.

Dr. Heyl: Is there any series of patients who have been followed on whom nothing has been done to treat the tumors?

Dr. Kahn: I do not know of any such series. Both the patients in the Mayo Clinic series who had only a biopsy died of the tumor. In view of the potential aggressiveness of these neoplasms I should not predict a happy outcome to such a policy. The results from x-ray therapy alone are conflicting, and the part played by x-ray therapy in the subsequent development of malignant change is not yet settled.

Dr. Heyl: This might be interesting. In 750 boys in a boys' school I have seen 10 to 15 cystic lesions a year in the x-ray films. Can giant-cell tumors be differentiated from simple cysts by a biopsy?

Dr. Lingley: The cysts usually occur in the diaphysis or metaphysis rather than in the epiphysis

and are seen usually before the epiphysis has fused. If an expanding cystic area occurs on the shaft side of the epiphyseal line it is more likely to be a benign cyst. In the epiphysis it is more likely to be a giant-cell tumor. Also, giant-cell tumors are somewhat rare in the age group seen by Dr. Heyl. They are more common between the ages of twenty and thirty-five years.

DR. KAHN: Only 10 of the patients in the Mayo Clinic series were under the age of twenty, and 2 of those were nineteen and 2 eighteen years.

DR. JOHN F. GIBBONS: I might ask Dr. Lingley if he thinks that sometimes a giant-cell tumor may have radiographic changes that strongly suggest a malignant tumor and the pathologist is unable to find evidence of malignant change. In those cases do you agree that one should recommend radical therapy?

DR. LINGLEY: Certainly, in this case the upper part of the cortex looks very ragged and suggests that the tumor might be malignant. I think it should be treated radically.

DR. KAHN: I do not know that we have any way of knowing whether disruption of the cortex indicates that the tumor is more aggressive or has been present longer. None of the published reports indicate that one can predict the subsequent course on the basis of this alone. I think one should understand that the giant-cell tumor is a distinct neoplasm with a high potential for local recurrence and a further potential for subsequent malignant change.

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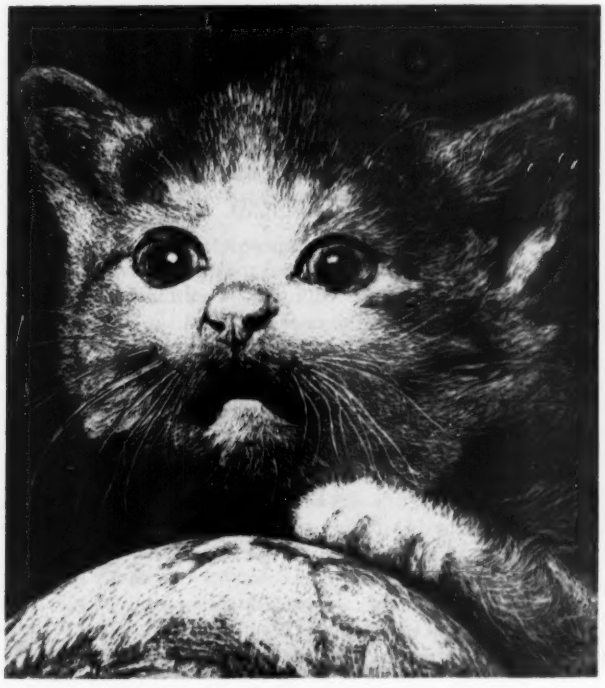

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Maxwell Finland, M.D. — Mark Aisner, M.D.
Vernon P. Williams, M.D. — Walter F. Lever, M.D.

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MEETING OF THE COUNCIL

THE Council of the Massachusetts Medical Society held a stated meeting on October 6 that proved to be an endurance contest of almost senatorial magnitude. The major discussion revolved about the controversial Medical Care Plan of the Massachusetts Department of Public Welfare; the heat engendered at times showed how exceedingly fortunate mankind has been in the abandonment of celluloid collars. Most of the discussion having taken place with the Council in executive session, reactions to the Plan were ventilated largely behind the veil of secrecy. The outcome of a very general discussion was the resubmission of the Plan to the Committee on Welfare Problems, with certain instructions from the Council to strengthen its position in trying to establish satisfactory relations.

The majority of committee reports were otherwise noncontroversial and were accepted in short order. The twentieth district medical society, confirming the new Charles River District, was announced as having been activated on August 4; by a simple act of geographic legerdemain the island of Nantucket was amputated from the Bristol South District and grafted onto Barnstable. Neither donor nor patient seems to have suffered any ill effects.

Resolutions were passed expressing the Council's appreciation of the activities of Dr. Laurence B. Ellis in connection with the Committee on Postgraduate Medical Education, and of the unique and valuable services rendered to the Society by Dr. John F. Conlin, in his capacity as director of medical information and education. The selection by the Executive Committee of Dr. Harvey A. Kelly, of Winthrop, as general practitioner of the year was unanimously approved.

"LOCAL MEDICAL DOCTOR"

Two correspondents whose letters appear elsewhere in this issue of the *Journal* make their own pertinent comments on the editorial "Vanishing American?" that appeared in the issue of August 12. The editorial, it will be recalled, reported the somewhat discouraging results of recent surveys conducted by the Massachusetts Academy of General Practice to determine the effectiveness of the efforts that have been made in promoting this vital branch of medicine.

Certain reasons for a falling off in the numbers of general practitioners become apparent with the knowledge that 111 of 744 replying to a questionnaire had inadequate hospital facilities and 29 had none whatever. Furthermore, departments of general practice in hospitals with adequate facilities were at the time of the survey available to only 159 physicians. Additional proof of the apparent unpalatability of the pudding was revealed by the discovery that whereas 44 per cent of first-year students indicated their intention of entering general practice, only 25 per cent were similarly minded in the fourth-year classes.

The factors that impel students to forsake their original ideals of service in this basic type of practice

are diverse; the letters of Captain Haubrich and Mr. Funk place special emphasis on the failure of many medical schools and their faculties to uphold the prestige of the general physician, and to include training for such a career in their concept of the undergraduate curriculum. One of these correspondents, in fact, deprecating the academic attitude toward the "L.M.D.," intimates that the majority of teachers are incapable of evaluating and appreciating the esteem in which general practice should be held, since they know nothing about it and may in some cases even hold it in contempt. The other suggests that only in those schools in which the general-practice preceptorship has been established do any large proportion of fourth-year students hold to their intention of entering this type of practice. The picture may have been drawn with lines that are too black, but it is the one that fits the common frame.

The terms "general practice," "general practitioner," "family doctor" and even "personal physician" slip easily from the tongue, but it may be that a renaming and a redefinition of this indispensable member of society will be necessary before even his professional colleagues know exactly whom and what they are talking about. The adjective "general" is in itself too vague to indicate anything in particular; as Webster says, it is not specific; not concrete; not precise or definite. It does not tell whether the physician so designated practices simple obstetrics, no obstetrics at all or all forms of obstetrics; whether he administers anesthetics, assists at operations, garners tonsils or occasionally performs an appendectomy, furtively or otherwise. His specializing brethren, who are supposed to know so much about so little, suspect him of being a jack of all trades and master of none; his lay patients, justly confused regarding his obligations to society and his capacity for discharging them may borrow their suspicious concept from the ultraspecialist or may regard him as their medical savior, ex officio.

Despite the results of any questionnaires, the "general practitioner" has come a long way in the last five years toward regaining his place in the sun. He has done much, as part of this progress, to identify himself and define his functions in the minds of both profession and laity, as witness the impressive paper on general practice by Collings and Clark in the issues of the *Journal* of January 22 and 29, 1953. The true stature and status of this modern physician are not yet fixed, however; he is still all things to all men in the eyes of those who live in the past of medicine, and something too far below this concept to many who do not appreciate the present complexity of medical practice or take sufficient thought of its future.

TUFTS COLLEGE MEDICAL SCHOOL LOOKS AHEAD

Tufts College Medical School, in line with the progressive policies that have characterized the sixty-one years of its existence, has announced a number of important changes designed to strengthen its curriculum, Dr. Charles G. Child, III, professor of surgery and chairman of the department, has accepted the appointment as director of the First Surgical (Tufts) Service at the Boston City Hospital, having resigned his position as surgeon-in-chief at the New England Center Hospital. The move will concentrate more of the Tufts surgical teaching at the City Hospital and aid in developing a high type of resident training at that institution. Dr. A. J. A. Campbell will continue as surgeon-in-chief of the Service, a position the prestige of which he has upheld through his personal attainments.

The previously separate departments of gynecology and obstetrics have been combined, with Dr. George W. Mitchell as professor of gynecology and chairman of the new department. Dr. Daniel J. McSweeney, formerly clinical professor of obstetrics at Boston University, has been appointed Tufts professor of obstetrics; Dr. Benjamin Tenney continues in the department as full professor of obstetrics at Boston University.

In addition to these progressive steps, of benefit both to school and to hospital, the opening of Posner Hall, the new dormitory for medical and dental students, has been announced. This building, providing up-to-date living quarters including recreation rooms and lounges, is situated on Harrison Avenue, only a half block from the schools.

"PHARMACY AND THE CONQUEST OF DISEASE"

Columbia University, in a way, celebrated this month three hundred and twenty-five years of progress by happily combining the bicentennial anniversary of the University itself and the hundred and twenty-fifth of its College of Pharmacy.

The occasion was signalized by a joint conference on Pharmacy and the Conquest of Disease held on October 14 and 15 at the McMillin Academic Theater, in which the modern chemistry of therapeusis really came into its own. Fittingly enough one of the world's most distinguished producers of pharmaceutical substances, George W. Merck, was moderator of the first morning meeting, being followed in the chair at the succeeding three sessions by Dean E. Emerson Leuallen, Leo Roon and Myron Walker. The modern uses of modern drugs were thoroughly discussed in all their aspects by a group of qualified speakers from every interested branch of science.

It seems especially appropriate that such an occasion should find manufacturers and merchandisers, public-health officers, clinicians and directors of research discussing their own contributions to the part that pharmacy is playing in the progressive conquest of disease. In these days of compromise and reasonableness drugless healing is no more to be tolerated than is heedless drugging.

A disposition is manifested, in high places, to attribute certain diseases to the agency of lead pipes. It is an annual affair, which generally subsides after a few remarkable cases have been shown to have had a different cause.

Boston M. & S. J., *Nov. 1, 1854*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

DAVIS — Stephen R. Davis, M.D., of Lynn, died on October 5. He was in his eighty-fourth year.

Dr. Davis received his degree from University of Vermont College of Medicine in 1896. He was a member of the staff of the Lynn Hospital and an associate fellow of the American Medical Association.

He is survived by his widow, a son, three daughters, five grandchildren and a brother.

EVANS — Albert Evans, M.D., of Boston, died on September 27. He was in his eighty-fifth year.

Dr. Evans received his degree from Harvard Medical School in 1902. He was a fellow of the American Medical Association and a member of the American Psychiatric Association.

He is survived by his widow.

LIEBMAN—William Liebman, M.D., of Boston, died on September 22. He was in his seventy-first year.

Dr. Liebman received his degree from Yale University School of Medicine in 1905. He was a fellow of the American Medical Association, a member of the New England Ophthalmological Society, and formerly chief of ophthalmology, Beth Israel Hospital.

He is survived by his widow, a daughter, a son, two brothers and a sister.

LYNCH — Cornelius J. Lynch, M.D., of Quincy, died on September 21. He was in his seventy-sixth year.

Dr. Lynch received his degree from Harvard Medical School in 1902. He was a director of the Tuberculosis Clinic of the Quincy Health Department and a member of the staff of the Carney Hospital.

He is survived by two nieces and five nephews.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1954

RÉSUMÉ

DISEASE	SEPT. 1954	SEPT. 1953	SEVEN-YEAR MEDIAN
Chancroid	2	2	2
Chicken pox	56	95	95
Diphtheria	1	1	4
Dog bite	1236	1064	985
Dysentery, bacillary	11	97	11
Encephalitis, infectious	1	0	2
German measles	39	58	58
Gonorrhea	198	191	217
Granuloma inguinale	0	0	0
Hepatitis, infectious	95	96	41†
Lymphogranuloma venereum	0	0	1
Malaria	2	2	2
Measles	275	24	69
Meningitis, meningococcal	10	5	3
Meningitis, Pfeiffer bacillus	1	2	2
Meningitis, pneumococcal	0	3	1
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	0	0
Meningitis, undetermined	7	3	3
Mumps	274	275	173
Poliomyelitis	352	177	156
Salmonellosis	20	17	11
Scarlet fever	59*	57	61
Syphilis	131	156	155
Trichinosis	3	1	4
Tuberculosis, pulmonary	214	176	189
Tuberculosis, other forms	17	10	9
Typhoid fever	3	3	1
Undulant fever	1	2	2
Whooping cough	184	186	268

*Includes streptococcal sore throat.
†Five-year median.

COMMENT

Diseases below the seven-year median were chicken pox, diphtheria, German measles and whooping cough.

The 56 cases of chicken pox reported represented the lowest figure for the month of September since 1922.

With but one exception (1952) the 184 cases of whooping cough reported represented the lowest figure for the month of September in the history of the State.

Diseases above the seven-year median included infectious hepatitis, measles, mumps, poliomyelitis and salmonellosis.

The increased incidence of measles this year was not unexpected since last year was the low point in the history of the State.

Mumps, however, continues at a high level in spite of a high year in 1953.

The situation regarding poliomyelitis is still not clarified. There is a general opinion, however, as mentioned previously, that a certain number of the cases masquerading this year as poliomyelitis may be due to other viruses.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

The following diseases were reported from the communities named:

Diphtheria: Boston, 1.

Dysentery, bacillary: Beverly, 1; Boston, 3; Lowell, 1; Oxford, 1; Southbridge, 1; Waltham, 4; total, 11.

Encephalitis, infectious: Wareham, 1.

Hepatitis, infectious: Arlington, 1; Billerica, 1; Boston, 5; Brockton, 3; Cambridge, 1; Chelmsford, 1; Chelsea Naval Hospital, 5; Concord, 3; Dracut, 1; Fall River, 25; Falmouth, 1; Fort Devens, 1; Haverhill, 2; Lowell, 5; Lunenburg, 3; Lynn, 1; Natick, 1; New Bedford, 1; Orange, 1; Quincy, 1; Somerset, 1; Somerville, 2; Springfield, 6; Sutton, 1; Warren, 1; Webster, 1; Westfield, 1; Williamstown, 9; Worcester, 10; total, 95.

Malaria: Fort Devens, 2.

Meningitis, meningococcal: Boston, 1; Chester, 1; Haverhill, 1; Holyoke, 1; Medford, 1; New Bedford, 1; Randolph, 1; Springfield, 1; Walpole, 1; Worcester, 1; total, 10.

Meningitis, Pfeiffer bacillus: Springfield, 1.

Meningitis, mumps: Quincy, 1; Southbridge, 1; total, 2.

Meningitis, undetermined: Boston, 2; Braintree, 1; Chelsea, 1; Marblehead, 1; Springfield, 1; Waltham, 1; total, 7.

Poliomyelitis: Agawam, 1; Andover, 1; Arlington, 2; Ashland, 2; Auburn, 5; Belmont, 3; Beverly, 8; Billerica, 1; Bolton, 1; Boston, 44; Bourne, 1; Boxboro, 1; Braintree, 3; Brockton, 1; Brookline, 2; Cambridge, 2; Carlisle, 1; Charlton, 1; Chelsea, 5; Chicopee, 1; Clinton, 1; Concord, 4; Danvers, 2; Dartmouth, 1; Dedham, 1; Dracut, 3; Everett, 4; Fairhaven, 2; Fall River, 4; Falmouth, 2; Fort Devens, 2; Framingham, 10; Gloucester, 2; Grafton, 1; Greenfield, 1; Hamilton, 1; Haverhill, 6; Holyoke, 2; Hopedale, 2; Hudson, 1; Hull, 1; Lancaster, 2; Lawrence, 8; Leicester, 2; Leominster, 3; Lexington, 2; Lowell, 7; Lynn, 16; Malden, 3; Marblehead, 2; Marlboro, 1; Marshfield, 2; Mattapoisett, 3; Maynard, 4; Medford, 1; Melrose, 1; Methuen, 2; Middleboro, 1; Milford, 2; Milton, 1; Montague, 5; Nantucket, 2; Natick, 2; Needham, 1; New Bedford, 4; Newton, 8; Northampton, 1; Norwood, 1; Otis Air Force Base, 2; Peabody, 3; Pittsfield, 1; Provincetown, 1; Quincy, 17; Randolph, 1; Reading, 1; Revere, 6; Rutland, 1; Salem, 7; Shirley, 2; Shrewsbury, 2; Somerville, 4; Southboro, 1; Southbridge, 1; Springfield, 1; Stoneham, 1; Stoughton, 1; Sturbridge, 1; Swampscott, 2; Taunton, 1; Topsfield, 1; Wakefield, 2; Waltham, 7; Wareham, 1; Wellesley, 2; West Boylston, 1; West Bridgewater, 1; West Springfield, 1; West-

field, 1; Weston, 2; Weymouth, 3; Williamstown, 1; Wilmington, 2; Winthrop, 9; Woburn, 6; Worcester, 27; total, 352.

Psittacosis: Boston, 1.

Salmonellosis: Boston, 7; Braintree, 2; Brockton, 1; Cambridge, 1; Dennis, 1; Greenfield, 1; Marblehead, 1; Medford, 1; Milton, 1; Newton, 2; Savoy, 1; Springfield, 1; total, 20.

Tetanus: Boston, 1.

Trichinosis: Boston, 2; Falmouth, 1; total, 3.

Typhoid fever: Ashland, 1; Haverhill, 1; Plymouth, 1; total, 3.

Undulant fever: Boston, 1.

CORRESPONDENCE

REGARDING THE "VANISHING AMERICAN"

To the Editor: Having just finished reading the editorial entitled "Vanishing American" in the August 12 issue of the *Journal* I thought that a student's thoughts on the problem might interest you.

Numerous factors influence today's student of medicine in his final decision on the type of medicine he will practice. Each year of his medical education adds to the decision.

The first-year student, by and large, enters medical school with only the haziest notion of the practical aspects of the practice and politics of medicine. He has probably been associated more closely with his family physician than with a specialist. Because of this, he has respect and admiration for the family physician and has, somewhere in his mind, an idea that he too would aspire to this type of medicine. However, forces have already been at work to change his mind.

His parents may have pointed out the long, hard hours of the family physician, who, he has noticed, drives a poorer car than the local surgeon or dermatologist. Probably, his friends and relatives have already begun to ask what specialty he is going into. If he answers that he has not thought of one and that so far general practice interests him, the same people often adopt the attitude that they would take toward an ignorant child who certainly should be guided by someone.

In his first year of medicine he is introduced to a tremendous amount of fact and an entirely strange language. At the same time no one reassures him that all of it cannot be learned immediately and that repetition is the backbone of the learning process.

He is taught anatomy by anatomists, physiology by physiologists, chemistry by chemists, and bacteriology by bacteriologists. These men, already specialized specialists, try hard to impress on the student the idea that theirs is foundation science in medicine.

He goes home in the summer with the idea firmly implanted that it is impossible to learn everything in medicine and that perhaps he should think of some specialized branch of medicine in the future. While at home he soon finds that his family physician cannot remember which percentage of the adult population has a palmaris-longus muscle and cannot give a very lucid explanation of the metabolism at the motor end plate in a muscle-nerve preparation. To make matters worse, the student is perhaps told that these facts are not important — in direct contradiction to what he has been taught for his first year by men of fame and learning.

The second year of medicine is usually the year in which the student is expected to absorb more knowledge in less time than ever before or again in his life. Again, he is taught pathology by pathologists, pharmacology by pharmacologists, and so on throughout his curriculum. Never once does he make contact with the general practitioner; if the term is mentioned, it is often in a deprecating or condescending manner.

School recesses and, once again, his family physician shows himself to be lacking in much basic material essential — or so the student has been informed — to the successful practice of medicine. Again, the family physician has been found wanting as compared to the famed teachers in the medical school.

At the same time family and friends keep up the incessant question, "What are you going to specialize in?" By now his answer is likely to be, "I haven't as yet made up my mind."

Now, the student begins his clinical years — his introduction to the practice of medicine. Surrounded by specialists at every lecture, during every ward round and in every teaching situation, he looks in vain for a general practitioner. Truly, this type of doctor has vanished from his idea of medicine.

The obstetrician points out the dangers of transverse arrest and the infinite skill required in version and extraction. The dermatologist excitably expounds on the obvious danger of overlooking a case of lupus erythematosus. The surgeon concisely gives statistical evidence of the Blalock I versus Blalock II procedure and can deftly accomplish both. By this time the student has decided that if he should ever have to do a version and extraction he must by all means be an obstetrician, that if he is never to miss a case of lupus erythematosus, years of dermatologic residency must be taken, and that certainly to do a Blalock either way he must buy a book of statistics and proceed to memorize it over a five-year period with a surgical residency thrown in for good measure.

It is also during this year that, on cases referred to the teaching centers, he is introduced to that abbreviation with its patronizing connotation—L.M.D. For some reason and in some manner, the local medical doctor or referring family physician is always made to resemble the local yokel from Podunk. His referring history and report of physical examination are always inadequate (after all, he neglected to do a galactose tolerance test on this patient with congenital heart disease!). His referring diagnoses are frequently treated with contempt by the physician in charge of the service and are nearly synonymous with the term—"ergo, ruled out." The student, of course, is left to form his own opinion of this man who cannot diagnose acinose-nodose tuberculosis when it stares him in the face.

After this year it is indeed a strong-hearted or weak-headed aspiring doctor-to-be who can still profess confidence and pride in his family physician. To that astounding 25 per cent who can still believe in general practitioners there is another year, tempered perhaps by a growing wisdom and a waxing cynicism — but, nevertheless, to be faced.

In his last year, in addition to pressures previously outlined, the student finds former schoolmates, whom he considered to be well informed, going into specialties and telling one and all that they are fools to work long hours, never being sure they are right, and gathering less remuneration than those in residencies will soon be earning.

Admittedly, this is a very rough sketch of some of the attitudes and pressures to which the student is subjected in medical school. Nevertheless, I believe that it is by and large what all present-day students must face and overcome if they are to become another vertebra in "the backbone of medicine."

JOHN W. FUNK
Fourth-year student
Aurora, Illinois

To the Editor: To help dispel the mystery of why the fourth-year medical student seems disinclined to fulfill his first-year aspiration to general practice, I submit the following observation.

Most of us are influenced to a remarkable degree, as the events that shape our careers fall into place, by the personalities with whom we come in contact. While learning the medical disciplines, the student is intimately associated with his instructors, and the present-day faculty is composed almost exclusively of an array of specialists. In the main this is as it should be. However, I have heard that schools in which the general-practice preceptorship has been incorporated into the fourth-year curriculum find a greater proportion of their seniors aspiring to the role of family doctor on completion of their training.

WILLIAM S. HAUBRICH
CAPTAIN, M.C.
Chief, GASTROENTEROLOGY SERVICE
Madigan Army Hospital
Tacoma, Washington

NOTICES

NUTRITION CONFERENCE

A conference on the subject "Nutrition Research in Progress," sponsored by the Massachusetts State Nutrition Committee, Massachusetts Dietetic, Home Economics and Public Health associations will be held at Simmons College, 300 Fenway, Boston, on Friday, November 5, and Saturday, November 6. The program on Friday will begin at 8:00 p.m., and that on Saturday at 9:15 a.m. There will be a charge for the tickets, which may be obtained from Mrs. Esther Factoroff, Simmons College, Boston.

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

A postgraduate course of eight panel discussions will be presented at the Mount Auburn Hospital, Cambridge, in Margaret Jewett Hall, 10:30 a.m. to 12 noon.

The course has been approved for credit by the Academy of General Practice. The program is as follows:

November 6. Acute Abdomen. Drs. Richard B. Cattell and Charles G. Child, III. Dr. Allan L. Davis, moderator.

December 4. Treatment of Peptic Ulcer. Drs. Franz J. Ingelfinger and Henry H. Faxon. Dr. Norman Zamcheck, moderator.

January 8. Office Gynecology and Endocrinology. Drs. George V. Smith and Somers H. Sturgis. Dr. Alexander A. Levi, moderator.

February 5. Congestive Heart Failure. Drs. Howard B. Sprague and Arnold S. Relman. Dr. Gordon A. Saunders, moderator.

March 5. Office Management of Diabetes. Drs. Alexander Marble and David Hurwitz. Dr. Harold L. Chandler, moderator.

April 2. Medical and Surgical Complications in Obstetrics. Drs. Duncan E. Reid, C. Sidney Burwell and James Metcalfe. Dr. Lloyd I. Sexton, moderator.

May 7. Office Management of Minor Surgery and Rectal Diseases. Drs. Thomas J. Anglem, Edwin Parker Hayden and Roy E. Mabrey. Dr. Gaspar Angelo, moderator.

MASSACHUSETTS PHYSICIANS ART SOCIETY

A meeting of the Massachusetts Physicians Art Society will be held at the headquarters of the Massachusetts Medical Society, 22 Fenway, on Thursday, November 4, at 7:30 p.m.

Mr. Anthony Milici will give a dissertation and demonstration in oils.

All members and other interested physicians are invited.

SOCIETY MEETINGS AND CONFERENCES

October, 1954–April, 1955. Postgraduate Medical Institute. Page 451, issue of September 9.

October 29. Edward K. Dunham Lecture. Page 679, issue of October 14.

October 29. Massachusetts Public Health Association. Fall Meeting. Blake's Restaurant, Springfield, Massachusetts.

October 30. Massachusetts Association of Medical Technologists. Page 679, issue of October 14.

October 31. Medical Television Program. March of Medicine. Page 631, issue of October 7.

October 31–November 4. American Institute of Dental Medicine. Page 968, issue of June 3.

November, 1954–May, 1955. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.

November 1, 1954–January 17, 1955. Hartford Medical Society. Page 496, issue of September 16.

November 1. New England Diabetes Association. Page 721, issue of October 21.

November 1–4. Interstate Postgraduate Medical Association of North America. Page 722, issue of October 21.

November 1–24. Consultation Clinics for Crippled Children in Massachusetts. Page 719, issue of October 21.

November 2–5. Fourth Annual Bay State Rehabilitation Conference. Hotel Statler, Boston.

November 2–6. National Society for Crippled Children and Adults. Page 631, issue of October 7.

November 3 and 4. M & R Pediatric Research Conference. Page 496, issue of September 16.

November 4. Massachusetts Physicians Art Society. Notice above.

November 5 and 6. Nutrition Conference. Notice above.

November 6. Massachusetts Hospital School Symposium. Page 495, issue of September 16.

November 6, 1954–May 7, 1955. Middlesex South District Medical Society. Postgraduate Course. Notice above.

November 11. Symposium on Chronic Pulmonary Disease. Page 721, issue of October 21.

November 11–13. American College of Cardiology. Page 722, issue of October 21.

November 12. Memorial Center for Cancer and Allied Diseases Conference. Page 544, issue of September 23.

November 12 and 13. Inter-Society Cytology Council. Page 968, issue of June 3.

November 15–19. American College of Surgeons. Page 496, issue of September 16.

November 15–26. Laboratory Diagnosis of Tuberculosis Course. Page 246, issue of August 5.

November 16 and 17. New England Diabetes Fair. Page 721, issue of October 21.

November 17. American Trudeau Society. Page 588, issue of September 30.

November 17. Massachusetts Academy of General Practice. Page 721, issue of October 21.

November 29–December 1. Association of Military Surgeons of the United States. Page 631, issue of October 7.

December 1, February 4 and April 8. Massachusetts Society for Research in Psychiatry. Page 679, issue of October 14.

December 3, 1954; February 4 and April 1, 1955. New England Society of Anesthesiologists. Page 1054, issue of June 17.

December 5. American Academy of Dental Medicine. Page 1092, issue of June 24.

December 7. Medical Television Program. The Doctor. (Cavalcade of America.) Page 631, issue of October 7.

December 8. New England Pediatric Society. Page 968, issue of June 3.

December 8. Postgraduate Seminar in Psychiatry and Neurology. Page 452, issue of September 9.

December 13–17. Congress of Obstetrics and Gynecology. Page 748, issue of April 29.

January 3–May 9, 1955. Postgraduate Seminar in Psychiatry and Neurology. Page 452, issue of September 9.

January 10–15. Course in Care of Atomic Casualties. Page 285, issue of August 12.

February 7–9. McIntyre-Saranac Conference. Page 410, issue of September 2.

February 11–25. Pan-American Academy of General Practice. Page 496, issue of September 16.

March 7–12. Course in Care of Atomic Casualties. Page 285, issue of August 12.

May 4 and 5. American Psychosomatic Society. Page 286, issue of August 12.

June 21–25. National Association for the Prevention of Tuberculosis. Page 540, issue of March 25.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 4

THURSDAY, NOVEMBER 4

National Society for Crippled Children and Adults. Hotel Statler, Boston.

M & R Pediatric Research Conference. Auditorium, State University College of Medicine, Syracuse.

Interstate Postgraduate Medical Association of North America. Municipal Auditorium, Minneapolis, Minnesota.

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.

*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.

*9:00–10:00 a.m. Cardiac Grand Rounds. Jimmy Fund Building, 35 Binney Street.

*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.

*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.

*12:00 m.–1:00 p.m. Surgical Staff Conference. Sherman Auditorium, Beth Israel Hospital.

*4:00–5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

*7:30 p.m. Massachusetts Physicians Art Society. Massachusetts Medical Society, 22 Fenway.

FRIDAY, NOVEMBER 5

National Association for Crippled Children and Adults. Hotel Statler, Boston.

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Dr. Proger and Staff. Stearns Auditorium, New England Center Hospital.

*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.

*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.

*4:00–5:00 p.m. Child Psychiatry. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

(Notices concluded on page xx)

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1. Buxton, C. L., and Vann, F. H.: New England J. Med. 236:536, 1948.
2. Douglas, H. S.: Western J. Surg. Obst. & Gynec. 59:238, 1951.
3. Cushny, A. R.: Textbook of Pharmacology and Therapeutics, ed. 10, Philadelphia, Lea & Febiger, 1943, pp. 436-437.

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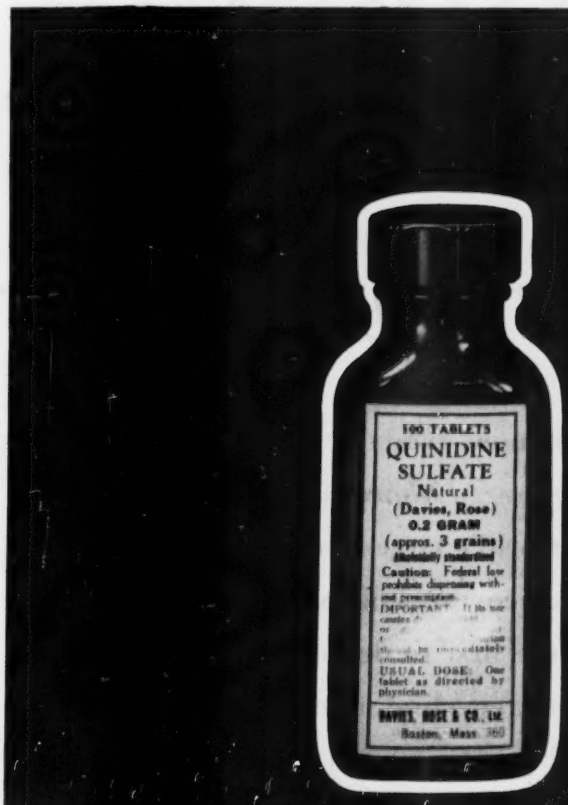

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NOTICES *(Concluded from page 758)*

5:00 p.m. Edward K. Dunham Lecture. Building C, Harvard Medical School, 25 Shattuck Street.
8:00 p.m. Nutrition Conference. Simmons College, 300 Fenway.

SATURDAY, NOVEMBER 6
National Association for Crippled Children and Adults. Hotel Statler, Boston.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.
9:15 a.m. Nutrition Conference. Simmons College, 300 Fenway.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
10:30 a.m.–12:00 m. Middlesex South District Medical Society Postgraduate Course. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.
*11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

MONDAY, NOVEMBER 8
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Therapeutic Conference. Dr. McCombs. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:00 p.m. Surgical Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
*7:00–8:00 p.m. Pathology Conference. Dr. MacMahon and Staff. Stearns Auditorium, New England Center Hospital.

TUESDAY, NOVEMBER 9
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:00 m.–1:00 p.m. Pediatric Combined Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Endocrine Clinic. Dr. Astwood. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic, New England Deaconess Hospital.
*4:00–5:30 p.m. Anesthesia Conference. Dr. Etsten. Stearns Auditorium, New England Center Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.

WEDNESDAY, NOVEMBER 10
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*11:00 a.m. Boston State Hospital Psychiatry Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th floor teaching unit, Beth Israel Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. Out-Patient Department.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*7:00–9:00 p.m. Postgraduate Seminar in Pediatric Neurology and Psychiatry. Cerebral Palsies. Drs. Clemens E. Benda and H. G. Brugsch. Walter E. Fernald State School, Waltham.
*7:30–9:30 p.m. Lahey Clinic Lecture. Joslin Auditorium, New England Deaconess Hospital.

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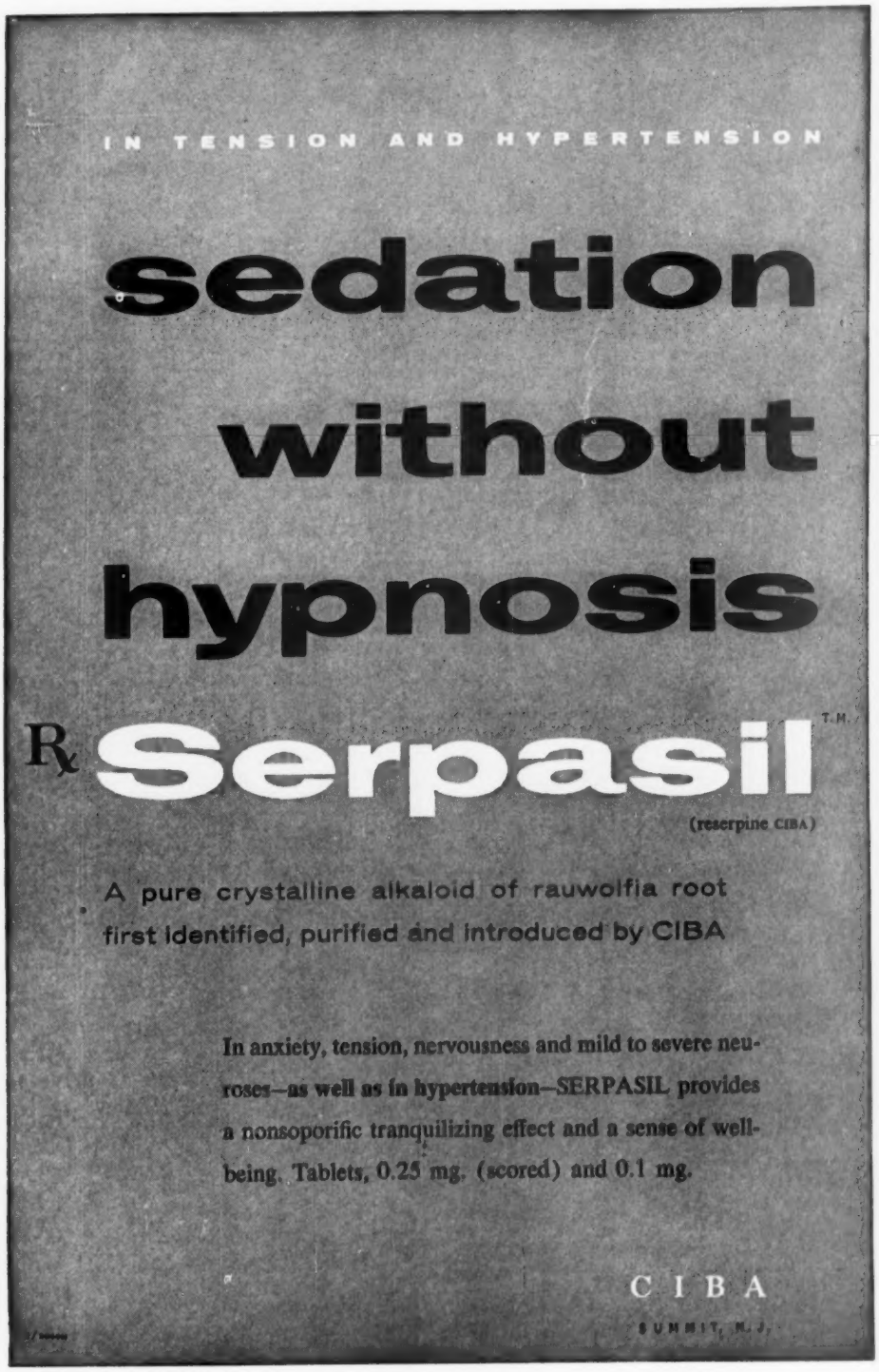
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1. Grayzel, H. G., Heimer, C. B., and Grayzel, R. W.: New York St. J. M. 53:2233, 1953.
2. Sobel, A. E. and Rosenberg, A.: 124th Meeting American Chemical Society, 1953